COMPARISON OF MR ENTEROGRAPHY WITH CT ENTEROGRAPHY IN PATIENTS WITH CROHN'S DISEASE

A DISSERTATION SUBMITTED IN PARTIAL FULFILLMENT OF MD RADIODIAGNOSIS (BRANCH VIII) EXAMINATION OF THE TAMIL NADU DR M.G.R. MEDICAL UNIVERSITY, CHENNAI, TO BE HELD IN APRIL 2017

DECLARATION

I declare that the dissertation entitled “Comparison of MR Enterography and CT Enterography in patients with Crohn’s disease” is my original work submitted in partial fulfilment of the requirement for MD Radiodiagnosis (Branch VIII) Degree Examination of the Tamil Nadu Dr M.G.R. Medical University, Chennai, to be held in April 2017.

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CERTIFICATE

This is to certify that the dissertation entitled “Comparison of MR Enterography and CT Enterography in patients with Crohn’s Disease” is the bonafide original work of Dr. Bernice Thamarai Selvi submitted in partial fulfilment of the requirement for MD Radiodiagnosis (Branch VIII) Degree Examination of the Tamil Nadu Dr M.G.R. Medical University, Chennai, to be held in April 2017.

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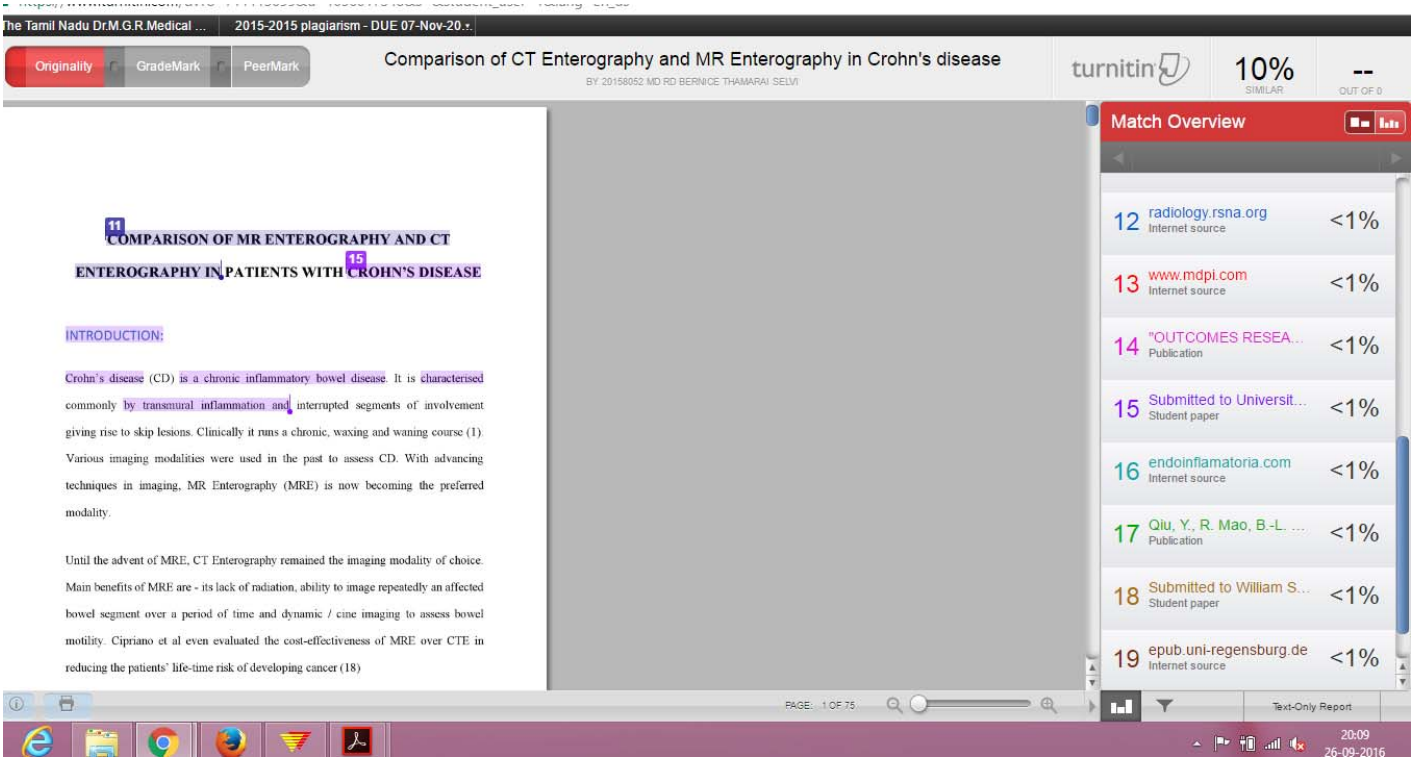
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Crohn's disease (CD) is a chronic inflammatory bowel disease. It is characterised commonly by transmural inflammation and interrupted segments of involvement giving rise to skip lesions. Clinically it runs a chronic, waxing and waning course (1). Various imaging modalities were used in the past to assess CD. With advancing techniques in imaging, MR Enterography (MRE) is now becoming the preferred modality.
Until the advent of MRE, CT Enterography remained the imaging modality of choice. Main benefits of MRE are - its lack of radiation, ability to image repeatedly an affected bowel segment over a period of time and dynamic / cine imaging to assess bowel motility. Cipriano et al even evaluated the cost-effectiveness of MRE over CTE in reducing the patients' life-time risk of developing cancer (18)
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COMPARISON OF MR ENTEROGRAPHY AND CT ENTEROGRAPHY IN PATIENTS WITH CROHN'S DISEASE

INTRODUCTION:

Crohn's disease (CD) is a chronic inflammatory bowel disease. It is characterised commonly by transmural inflammation and interrupted segments of involvement giving rise to skip lesions. Clinically it runs a chronic, waxing and waning course (1). Various imaging modalities were used in the past to assess CD. With advancing techniques in imaging, MR Enterography (MRE) is now becoming the preferred modality.

Until the advent of MRE, CT Enterography remained the imaging modality of choice. Main benefits of MRE are - its lack of radiation, ability to image repeatedly an affected bowel segment over a period of time and dynamic / cine imaging to assess bowel motility. Cipriano et al even evaluated the cost-effectiveness of MRE over CTE in reducing the patients' life-time risk of developing cancer (18)

We aim to compare the 10 described mural and extra-mural findings in Crohn's disease on CT Enterography with MR Enterography.

AIMS AND OBJECTIVES:

1. To compare the sensitivity and specificity of MRE and CTE in patients with active Crohn's disease by assessing the ten mural and extra-mural findings described in Crohn's disease

2. To optimize the MRE protocol by prioritizing the sequences, so that it is cost effective and less time consuming.

3. To make MRE the imaging modality of choice for children and young adults with CD, who require repeated imaging.

JUSTIFICATION FOR THIS STUDY:

The need for this research is to establish & optimize the technique of MRE. At present, CTE is more readily performed for small bowel pathologies. MRE will benefit children and young adults by eliminating the long term effects of ionizing radiation due to repeated CT scans.

The limitation faced with MRE at present is the longer scan time, cost & decreased patient compliance in the form of breath hold for the MRI sequences, compared to CT. Therefore

one of the objective of my study is also to optimize the protocol, that with fewer sequences, comparable results can be obtained.

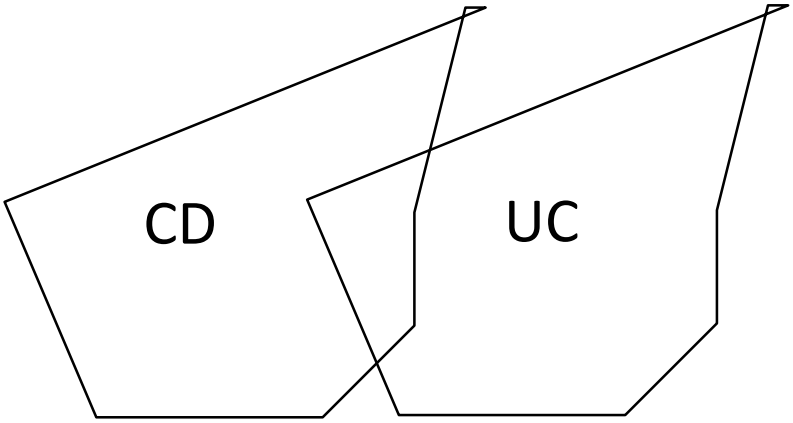
REVIEW OF LITERATURE:

CD was initially called regional enteritis or terminal ileitis. Symptoms similar to CD were reported by physicians as early as the 17th century. It was first recognised and described by Crohn, Ginzburg and Oppenheimer in 1932. It was later distinguished from UC in 1959 based on clinical, histological and radiological features.(2)

There is no single attributable factor for this disease. Genetic susceptibility, luminal antigenic drive and environmental triggers predispose to this condition.

CD is one of the inflammatory bowel diseases, the other being ulcerative colitis (UC). These are chronic, idiopathic conditions. Both CD and UC share clinical picture and therapeutic responses and in some patients may it may not be possible to distinguish between the two.(3)

Intermediate colitis



Clinical features and pathophysiology:

Patients usually present with chronic intermittent diarrhoea, abdominal pain – diffuse / right lower quadrant, low-grade fever, chronic fatigue, weight loss. Small bowel involvement in CD present with malabsorption, weight loss and anorexia.

Perianal CD may have debilitating perirectal pain, foul smelling discharge from fistulae (1)

Inflammation, edema and spasm of bowel wall may cause symptoms of subacute bowel obstruction. Chronic disease with fibrosis may cause complete obstruction.

Although any part of the GIT may be affected, ileo-cecal region is the most frequently affected, followed by the small bowel alone and colon (1)

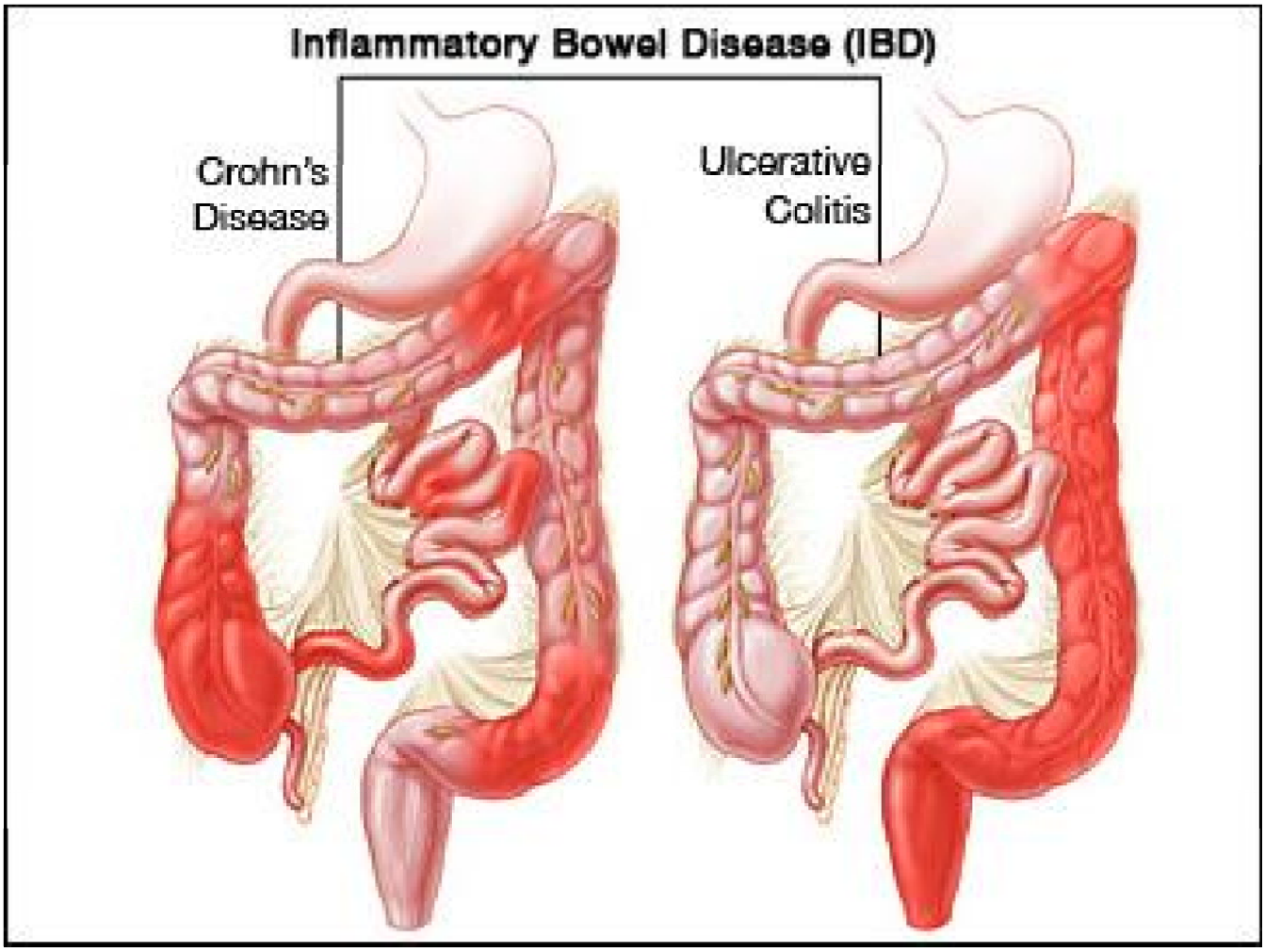


Diagram depicting the distribution of CD versus UC in the GIT (1)

Chronic or recurrent disease present with hematochezia, ascites, significant weight loss, abdominal lump. Chronic indolent course may last for more than a year (1)

Ileum is involved in 45 %, colon 20%, small bowel 33 %, and gastro-duodenal and perianal region 5% in the form of fistula, abscess, ulcer or stricture, or fissure.

Extra-intestinal manifestations include pancreatitis, sacro-iliitis(1)

In pediatric population, growth failure may manifest before the onset of GI symptoms(1)

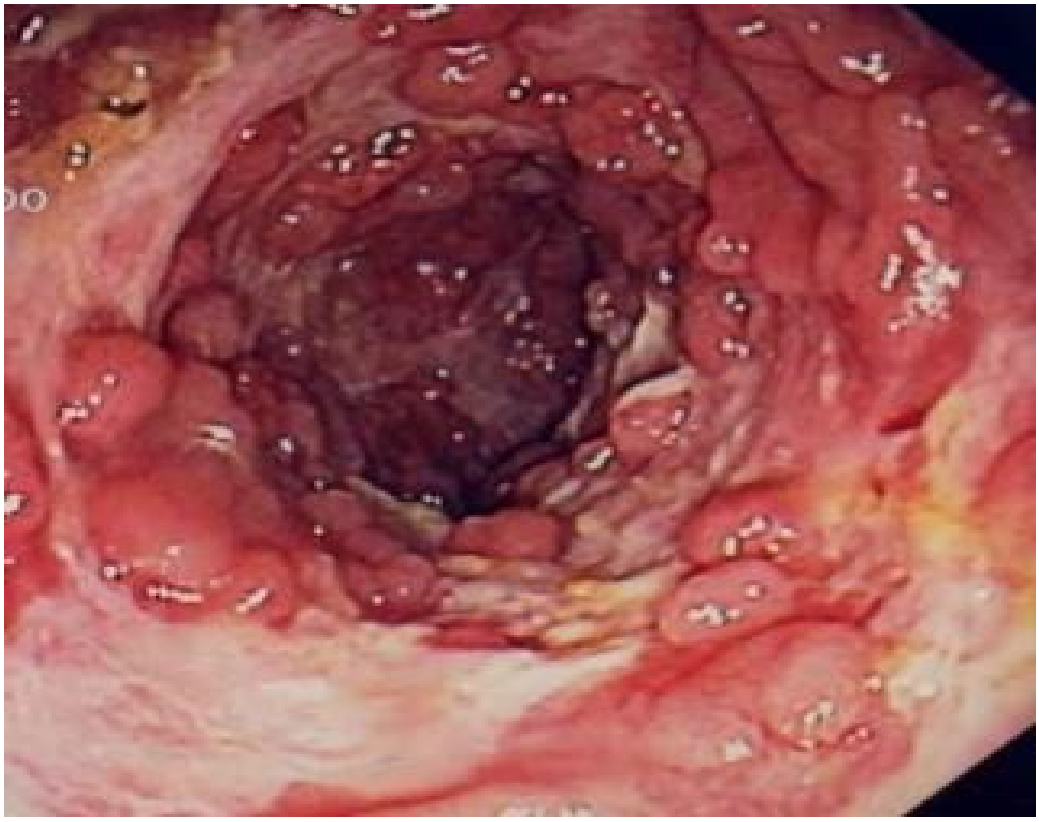
Laboratory features:

Lab results are non-specific for CD. However, surrogate markers for presence of inflammation, nutritional status can be assessed. Features that may be present are:

Anaemia, hypoproteinemia and elevated erythrocyte sedimentation rate, raised CRP. (4)

Endoscopy findings:

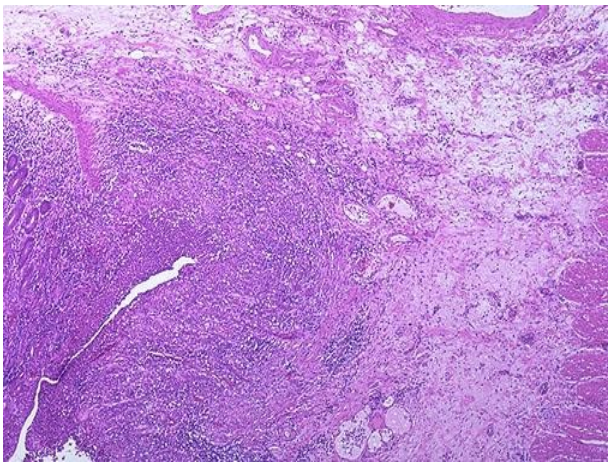
Skip lesions, aphthous ulcers, fissures, fistula, cobble-stone appearance of mucosa and stricture(4)

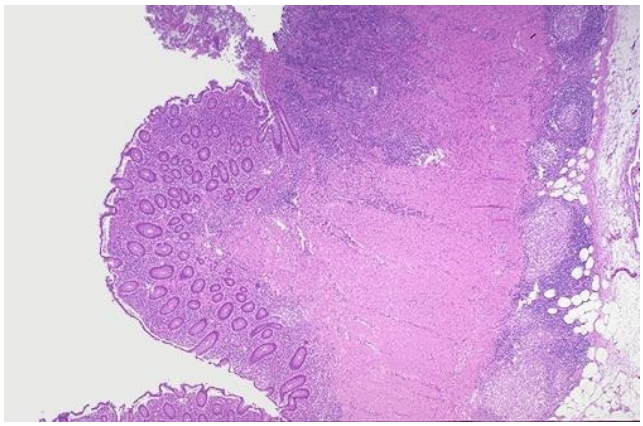


Colonoscopy image depicting cobblestone mucosa. (1)

The histological features include: presence of granuloma - caseating or confluent,

4)





epithelial ulcers, crypts, lymphoid aggregates. In a country like India, where TB is prevalent, it is crucial to differentiate CD from TB. Large, dense and confluent caseating granulomas in mucosa or sub-mucosa, involvement of more than four sites of granulomatous inflammation, caseation, band of epitheloid histiocytes in the base of the ulcer and granulomatous inflammation in cecum suggest histo-pathological diagnosis of TB. Whereas presence of small, discrete non-caseating granuloma in mucosa, mucosal changes distant to sites of granuloma, cryptitis, crypt abscess and granuloma in sigmoid or rectum are in favour of histopathological diagnosis of CD.(3,

A. Deep fissure extending from mucosa to submucosa. (4)

B. Transmural inflammation in mucosa, submucosa, nodular infiltrates in the serosal layer (4)

Diagnosis:

Morphological and pathological features that are diagnostic for CD are as follows.

These features correlate well with radiological, endoscopic or surgical findings.

- Morphological:

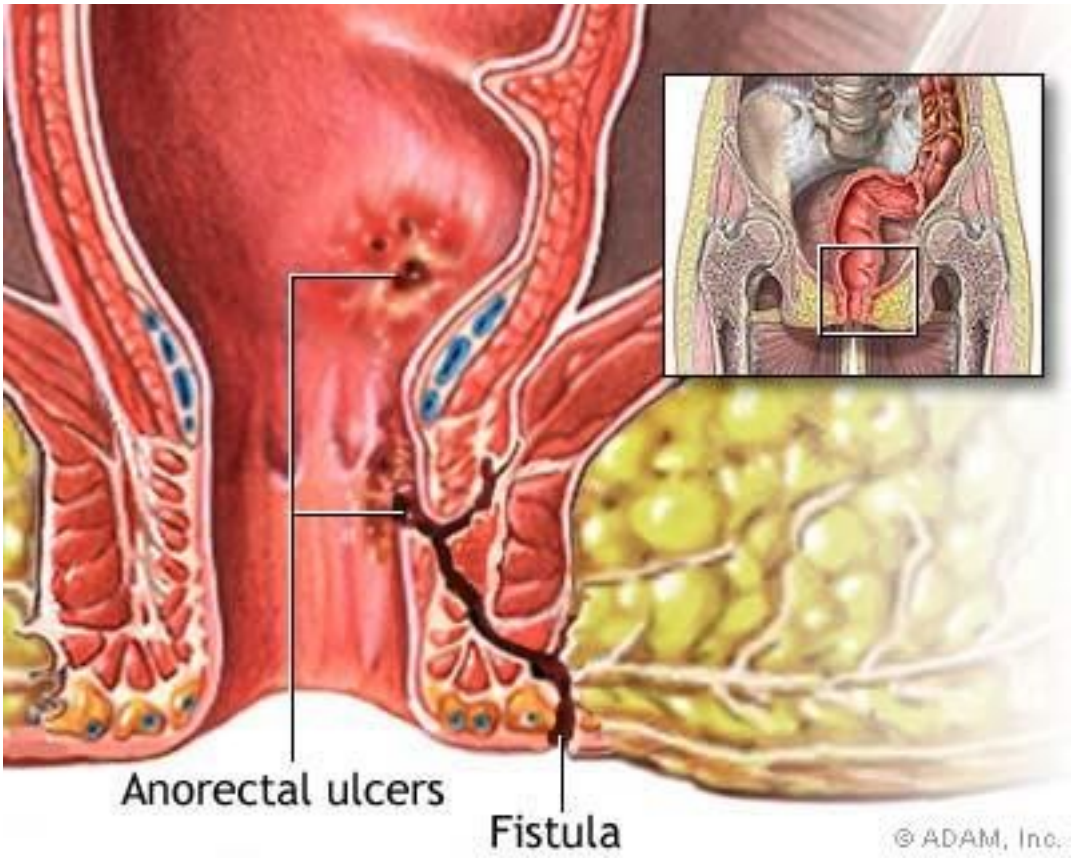
(a)skip lesions

(b) deep mucosal longitudinal fissures / ulcers

(c)transmural inflammation

(d) fibrotic or rigid bowel wall or strictures

(e)fistulizing disease - entero-cutaneous / entero-enteric and / or chronic perianal disease.



Anatomical drawing depicting fistulizing perianal disease. (1)

- Histopathological criteria for diagnosis:

Goblet cells with normal mucus in the inflamed mucosa, mucosal and submucosal lymphocytic aggregation, non-caseating granuloma, longitudinal ulcers / fissures and transmural inflammation

In a country like India, where TB is prevalent, and with similar clinical and radiological profile, a definite diagnosis of CD should be made, with exclusion of TB.

Overall diagnostic criteria for CD are:

- presence of at least 3 different morphological criteria

- presence of non-caseating granuloma on histology

- and at least 1 other criterion; excluding TB (based on histology, microbiological and PCR studies) and treatment response (as evidenced on endoscopy and histology) after 1-year of treatment with corticosteroid and 5-ASA preparations (with or without surgery).(4)

Epidemiology:

The burden of Crohn's disease in the United States and other western countries are almost similar. The incidence is reported to be up to 5/100,000 population and the prevalence is 50/100,000 (6)

The overall disease burden in the Asia-Pacific region is found to be lower than that in the North America and European countries. There is no specific data regarding the frequency and determinants of this disease in India. In a retrospective community based study in different countries, the minimum incidence is reported to be

0.14/1,000,000 per year (7)

In an article published in the Indian Journal of Gastroenterology, 223 patients with proven Crohn's disease were studied in our institution from Jan 1995 to Dec 2008 (8)

The incidence and prevalence of Crohn's disease in the Indian immigrants in the UK was found to be 4.39/1,000,000 per year compared to the general population which is 7.47/1,000,000 per year as in 1980-1985 (9). Recently mutations in NOD2/CARD15 gene, which is present in IBD1 locus on chromosome 16 were found to be associated with CD (6). There are three mutations recognised in NOD2 gene in patients with CD in the west. However, none of these are seen in the Indian population with CD (7)

The age of onset in most cases of Crohn's disease is between 15 and 40 years and a slight female predominance(10). The peak age of Indian patients with CD is 30 – 40 years, according to The Task Force on Inflammatory Bowel Diseases (IBD) of the Indian

Society of Gastroenterology published in 2012(7).

The diagnosis of CD should be based on a combination of clinical, endoscopic, histological, and radiological features and with satisfactory exclusion of tuberculosis and other infective causes(7). CD accounts for nearly 65% of cases of pediatric IBD (8)

Clinical classification and current concepts in Crohn's disease activity (19)

With better knowledge about genetic and environmental influence on CD, there is wide variation regarding – disease location, severity of the disease, treatment response and behaviour of the disease. Clinical classification helps identify the different phenotypes into those who have chronic stable disease and others with penetrating disease complications. Clinical classifications like Vienna and

Montreal classifications recognize the pattern of disease process, thereby specific therapies can be tailored, to predict future complications and offer surgical management at the appropriate time.

Vienna Classification for Crohn's Disease activity

Age at diagnosis	A1: < 40 years A2: = / > 40 years
Location	L1: Terminal ileum L2: Colon L3: Ileo-colon L4: Upper GI
Behaviour	B1: Non-stricturing, Non-penetrating B2: Stricturing B3: Penetrating

In the modified Montreal classification, penetrating perianal disease was also included. Perianal penetrating disease like fistulas and abscesses have different prognosis compared to intra-abdominal penetrating disease.

Patients may remain in the same category or progress from inflammatory to structuring to penetrating.

Treatment options for various clinical types:

Inflammatory type	Mostly medical management
Stricturing type	Medical and interventional – balloon dilatation / stricturoplasty / resection
Penetrating type	Mainly surgical management

IMAGING TECHNIQUES IN CROHN'S DISEASE:

1. Barium meal follow through
2. Barium / CT enteroclysis (when contrast is instilled via nasojejunal tube to distend the bowel, followed by fluoroscopy or CT)
3. CT or MR enterography where patient drinks a large volume of contrast to achieve bowel distension followed by CT or MRI.
4. Routine CT with IV contrast and MRI with IV contrast – in appropriate settings

Of these, enterography technique is superior in achieving adequate bowel distension. Since NJ intubation is not required in enterography, compared to enteroclysis, this is less invasive with better patient tolerance.

ENTEROGRAPHY:

Enterography can be done either with CT or MRI.

CT enterography, since first introduced by Raptopoulos et al in 1997, has been the imaging modality of choice, to assess small bowel pathology in detail, especially to assess the extent and severity of Crohn's disease. Similar techniques have been introduced subsequently. These are broadly termed CT enterography (where patients drink oral contrast) and CT enteroclysis (luminal contrast is introduced via a nasojejunal tube placed fluoroscopically prior to CT examination). (2)

Adequate small bowel distension is essential to assess wall thickening and mural enhancement. (11)

CTE technique:

Patients are asked to fast overnight. Tab Itopride 50 mg is first given to promote gastric motility and emptying prior to taking oral contrast. After about 15-20 minutes, approximately 1.5 litres of oral contrast, which is Peglec (Polyetyhlene Glycol)

dissolved in drinking water is consumed over a period of 45 minutes to 1 hour. Peglec distends the bowel and renders neutral luminal contrast, which allows good visualisation of bowel wall. Following this, 20 mg of Buscopan (Hyoscine Butyl Bromide) is administered IV, to decrease bowel motility. CT scan is performed with 80 ml of iodinated IV contrast is given through a pressure injector. Axial sections of the abdomen – from the domes of the diaphragm to the pubic symphysis are acquired in the arterial and venous phases and coronal reconstructions are done.

MR Enterography:

Cross-sectional imaging like CT and CTE plays an important role in the evaluation of small bowel pathology. With increasing awareness of radiation risks among the medical field and general public, radiation-free imaging techniques like MRE are considered as safe alternatives. However, for initial imaging, CTE is still preferred, except for young patients. For follow up imaging, MRE is preferred than CTE. In fistulising perianal disease, MRE can be combined with high resolution sections of the perineal region for complete evaluation in a single sitting (12)

Advantages with MRE: (9)

- Lack of ionizing radiation

- Dynamic assessment is possible, regarding bowel distension and motility. Affected segment can be assessed during different phase of the study

- Improved soft tissue contrast

- MR IV contrast is relatively safer compared to iodinated contrast

Limitations of MRE (9):

- Limited availability and expertise in performing and interpreting the study - Cost

- Longer scan duration requiring breath-hold, which may be difficult for some patients

- Comparatively decreased spatial and temporal resolution to CT

- **Indications (9):**

- Primary indication is for children and young adults with CD – in whom radiation is a concern, since they require repeated imaging.

- Patients with absolute contraindication for CT

- Patients with low grade small bowel obstruction

MRE technique:

Patient preparation, consuming neutral oral contrast and use of Buscopan are same as for CTE, which was described above. Instead of CT, MRI with IV Gadolinium is done.

Enteric contrast agents for MRE (9):

Based on the signal intensity on T1 and T2 weighted imaging, the oral contrast agents are classified as positive – bright on both, negative – dark on both, biphasic – bright on one and dark on the other. Biphasic is most often used, which includes water, polyethylene glycol, barium sulphate, locust bean gum, methyl cellulose and mannitol.

MRE oral contrasts: Biphasic agents and their limitations (12)

Water	Rapidly absorbed. Poor distension
Polyethylene glycol	Rapid transit, Strong urge to evacuate, Diarrhoea
Diatrizoate meglumine and sodium salts	Diarrhoea
Methyl Cellulose	Availability
Barium Sulfate	Taste

MRE oral contrasts: Negative agents and their limitations (12)

Ferumoxsil oral suspension	Taste, Distension, Cost
Oral Superparamagnetic particles	Availability
Perfluoro-octyl bromide	Availability

MRE oral contrasts: Positive agents and their limitations (12)

Gadolinium chelates	Cost
Manganese	Availability
Food substances (blueberry juice, milk, ice cream, green tea)	Storage and administration

MR imaging (9):

Patients are usually imaged in supine position. Imaging in prone position provides separation of small bowel loops and decreases the thickness of the body to be imaged. Administration of a spasmolytic like Buscopan decreased peristalsis and thereby motion artefacts. Gadolinium based IV contrast is used to detect areas of

hyperenhancement, indicating active inflammation. Imaging is begun 45 seconds after injection of contrast.

MRE imaging sequences (9):

Sequence	TR , TE (m sec)	Matrix	Slice thickness, gap mm	Advantages	Limitations
HASTE	2000, 90	256 x 256	5/0	Few susceptibility artefacts.	Intraluminal artefacts
Bal SSFP without FS	3.8, 1.7	192 x 340	5/0	Mesenteric visualisation	Suscep and band artefacts
Bal SSFP with FS	3.8, 1.7	192 x 340	5/0	Mural and perienteric inflmatn.	-
2D ultrafast grad echo	200, 3.8	320 x 160	6/0	Sharp bowel wall	Respiratory artefacts
3D ultrafast grad echo	5-2, 2.5	384 x 224	4/0	Bowel tracking	Blurred walls

By combining the sequences, the limitations of one is compensated in the others. Balanced SSFP better depicts lymph nodes. Fat suppressed sequences improves contrast between hyperintense inflamed bowel wall from dark perienteric fat.

Recommended MRE protocol includes (9):

- Coronal HASTE (Half-Fourier Acquisition Single-Shot Turbo Spin Echo)

- Balanced SSFP (Steady State Free Precession) without fat suppression – coronal and axial

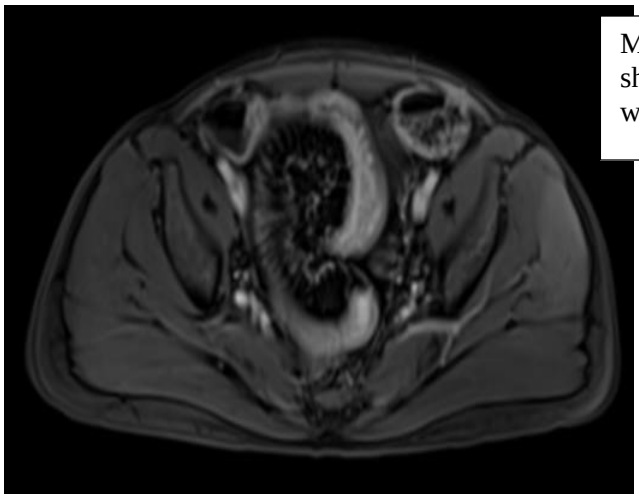
- Balanced SSFP (Steady State Free Precession) with fat suppression in axial

- 2D and 3D ultrafast gradient echo – in axial and coronal, pre and post-contrast

MR Enterography findings in Crohn's Disease (9):

Several studies have shown that MRE has high sensitivity for diagnosing and grading the severity of the disease and differentiating active inflammatory, penetrating / fistulising disease and fibrostenotic disease.

ucosal hyper-enhancement compared to adjacent unaffected bowel is one of the earliest signs of active inflammation. This finding may appear even before wall thickening. Mucosal enhancement with submucosal edema causes stratification. The presence of serosal enhancement also, gives a 'target' appearance (9).



MRE - Axial T1 VIBE post contrast image showing mucosal hyperenhancement and wall stratification

The sensitivity & specificity of MRI for the detection of CD range from 88 – 98 % and from 78 – 100 % respectively(13).

MRE interpretation:

Ten characteristic mural and extra-mural imaging features are seen in CD as follows (15).

- **Mural thickening**: single wall thickness measuring > 3mm

- **Mural stratification**: enhancing mucosa and submucosal edema and serosal enhancement

- **Skip lesions**: Multiple discontiguous segmental involvement, with intervening normal bowel

- **Luminal stenosis and luminal dilatation**: Abrupt change in calibre of the lumen, persisting during various sequences during the examination

- **Phlegmon**: enhancing soft tissue in the mesentery, adjoining an affected segment of bowel.

- **Fistula**: entero-cutaneous, entero-enteric, entero-vesical

- **Abscess**: extraluminal collection, with enhancing walls

- **Lymph nodes**: measuring > 10 mm in short axis diameter, with or without enhancement

- **Creeping fat**: Fat proliferation along the mesenteric border of the affected bowel segment. These areas may show prominent vasa recta (14)

CTE versus MRE: Advantages and disadvantages.

FACTOR	CTE	MRE
Spatial resolution	Better than MR	Lesser than CT
Motion artefacts	Fewer	More
Availability	More	Less
Cost	Less expensive than MR	Expensive
Examination time	Shorter (10 minutes)	Longer (30-40 minutes)
Claustrophobia	Nil	May be present
Ionizing radiation	++ Mean CTDI for CTE 4.9 mGy	Nil
Soft tissue contrast resolution	Lower than MR	Excellent
Dynamic bowel imaging	Not feasible	Feasible
Differentiating acute vs chronic disease	Not always reliable	Reliable with DWI sequence

Similar studies in literature:

Up to three different studies compared CTE and MRE in small bowel pathologies and CD.

1. Amittai et al compared the sensitivity and specificity of CTE and MRE in CD. 42 biopsy proven cases of CD were assessed based on the 10 mural and extra-mural findings. However, the CT and MR were performed within an average period of 6 weeks between them. Their study, published in IMAJ in 2015 showed > 70% agreement between CTE and MRE in detecting 8 out of 10 signs, and <70% in detecting luminal dilatation and adenopathy. This study used the standard of reference as combined positive findings on both tests. Creeping fat sign and fistula were better detected on MRE than CTE. Their study concluded that both CTE and MRE has comparable diagnostic accuracy CD, even with a time interval of upto 6 weeks (15)

2. Jensen et al studied 50 patients with known Crohn's disease, by performing CTE and MRE on the same day, MRE prior to CTE. They correlated with ileo-colonoscopy or surgery as the gold standard. In this study published in the Scandinavian Journal of Gastroenterology in 2011, they concluded that both CTE and MRE have reliable diagnostic accuracies. Also in their study, in patients with active disease, PPV were favourable, but low NPV. Therefore, a negative CTE or MRE should be cautiously interpreted. (16)

3. Siddiki et al studied 33 patients who were scheduled for CTE and ileo-colonoscopy also underwent MRE. In the final result, biopsy and clinical assessment were also

included. 23 of those had both MRE and CTE on the same day and the remaining had MRE within 21 days after CTE. Their results showed that perfect agreement was seen with mural stratification on MRE and hyperenhancement seen on CTE. Comb sign has almost-perfect agreement between the two. Quality score was higher with CTE. However, they compared only 3 signs. This study published in AJR in July 2009 also concluded that MRE is an accurate technique and preferred imaging modality for patients with small bowel CD

4. Other studies by Lee et al who evaluated 6 signs and Fiorino et al also found good agreement between the two modalities

ACR (American College of Radiology) recommendation:

Based on the ACR appropriateness criteria, the recommended imaging investigation between CT Enterography (CTE) and MR Enterography (MRE) in Crohn's disease is as follows (17)

1. For an adult, when the initial presentation is acute, with severe abdominal pain, fever, leucocytosis, vomiting, otherwise stable, CTE or CT abdomen scores over MRE – mainly due to shorter scan time and due to improved sensitivity to detect free intra-peritoneal air. If the patient has contraindication to iodinated contrast, then a routine MRI – pre and post contrast is recommended over MRE

2. For an adult patient, when the initial presentation is indolent, mild to moderately symptomatic – with abdominal cramps, suspected Crohn's disease, CTE and MRE are considered equivalent alternatives, with MRE having the advantage of lack of ionizing radiation

3. For a child with initial presentation of suspected Crohn's disease, MRE is the preferred choice, followed by CTE as the second choice

4. Adult with known Crohn's disease, having an acute episode of fever, increasing abdominal pain, CTE is the preferred test. If unable to tolerate the oral contrast ingestion required, then routine CT abdomen with IV contrast is recommended.

5. Child with known Crohn's disease, having an acute episode of fever, increasing abdominal pain, MRE is the recommended test

6. Adult or child, with known Crohn's disease, clinically stable, with mild symptoms, MRE is the recommended modality

Methodology:

Approval for the study protocol from the institutional review board and ethics committee of IRB was obtained (IRB minute number: 9965, dated 2.3.2016). 25 patients with clinical suspicion of Crohn's disease, who fulfilled the inclusion criteria were recruited in the study, after getting informed consent. The study group consisted of 21

men and 4 women, age ranging from 18 to 49 years, with a mean age of 32.12 years. The patients underwent MR enterography and CT enterography on the same day. The images were read by two independent radiologists. 10 mural and extramural findings, namely: bowel wall thickening, wall stratification, enhancement, stenosis, dilatation, fistula, phlegmon, skip lesions were looked for.

Endoscopy findings, histopathological findings of biopsy specimens were compared for the final analysis. We also assessed the degree of bowel distension, artefact score, extra-enteric findings like inflammatory arthritis and comparison made with previous imaging if any. Treatment details, and relevant co-morbidities were also looked into.

Participants: Patient selection is based on the inclusion & exclusion criteria

Inclusion criteria:

– All patients with proven active Crohn's / high degree of clinical suspicion for CD, who are scheduled for CTE and consented for MRE were included in the study.

Exclusion criteria:

- Any patient with absolute contraindication to CECT: pregnancy, renal insufficiency, documented adverse reaction to iodinated contrast agents,

- Any contraindication to MR imaging: cardiac pacemakers, otic implants, ferromagnetic aneurysm clips or heart valves, severe claustrophobia

- Suspected bowel obstruction

- Post-op patients with stoma

SAMPLE SIZE CALCULATION:

Diagnostic Test - Comparing the sensitivity of the new test with reference test	
Sensitivity/Specificity of the new test (%)	85.7
Sensitivity/Specificity of the reference test (%)	95.2
Difference	9.5
Power (1- beta) %	80
Alpha error (%)	5
1 or 2 sided	2
No. of diseased subjects needed	**149**

With reference to *AJR* 2009; 193:113–121. The sensitivity of MR was found to be 85.7% and CT was 95.2% respectively with a power at 80% and alpha error at 5% for a two sided test we need to study at least 149 cases.

Statistical method:

The sensitivity, specificity, and predictive values will be analysed for MR and CT. Agreement between MR and CT finding will be done using Kappa statistics.

Research plan:

Setting & locations: Study was conducted in the Department of Radiodiagnosis,

ASHA radiology extension, CMC, Vellore, On 1.5 Tesla MRI scanner (Siemens

Avanto Fit)

18 element body coil

Recruitment: All patients who were scheduled for CTE between December 2015 to August 2016, and who met the inclusion criteria and consented for the study were recruited.

There was good inter-departmental co-operation from clinical gastroenterology department (GEC) for this study.

Procedure:

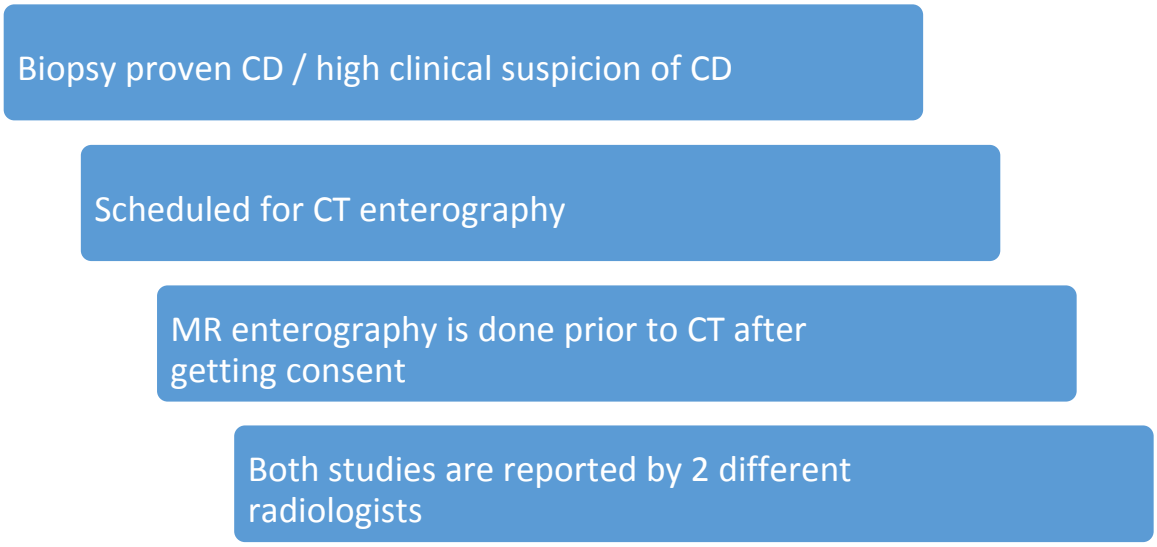
When the patient reports to the CT room to undergo the scheduled CTE, the patient was informed about this ongoing study and requested to participate. An information sheet regarding MRE in the language understood by the patient was also provided. If the patient consents, they were included and the patient's signature taken in the consent form.

After confirming the fasting state, the patient is given a tablet Itopride 50 mg. After 15 minutes, the patients were instructed to consume the oral contrast over a period of 45 minutes to 1 hour. The oral contrast is a solution of Peglec dissolved in 1.5 litres of drinking water. The need to drink this at regular intervals was stressed upon to ensure uniform bowel distension. Markings were made on the bottle to ensure the same.

By marking 4 divisions on the bottle, patient's compliance improves to consume steadily. This will ensure uniform bowel distension.

Patients were instructed to with-hold approximately 1 cup of the contrast. By the end of about 45 minutes, when most of the contrast has been drunk, 2 ml of Inj. Buscopan was given intravenously to decrease the bowel motility. Immediately the patient was taken to the MRI scanner and the study was performed. After the MRI, the patient was instructed to drink the remaining 1 cup of oral contrast and CTE is done. The CT and MRI suites are adjoining in location. Both the exams were archived to the PACS and is made available for viewing and reporting.

Diagrammatic Algorithm of the study:



MRE protocol used for this study:

As mentioned earlier, the MRE were performed on 1.5T Siemens Avanto Fit MRI scanner. 18 (2 x 9) element body coils and a respiratory bellow were placed to assess breath-hold. Even though 12-14 different sequences were described in the literature, we limited our sequences to 9

1. Tru FISP coronal: (TR 2000 ms, TE: 90 ms, FOV 380 mm, Matrix: 99 x 160, Slice thickness: 3 mm)

2. T2 Coronal: (TR 687 ms, TE: 2.2 ms, FOV 320 mm, Matrix: 273 x 272, Slice thickness: 4 mm)

3. T2 Axial: (TR 519 ms, TE: 2.14 ms, FOV 380 mm, Matrix: 196 x 256, Slice thickness: 3 mm)

4. VIBE Axial Pre and post-contrast: (TR 4.49 ms, TE:2.16 ms, FOV 380 mm, Matrix: 182 x 320, Slice thickness:3 mm)

5. VIBE Coronal Pre and post-contrast: (TR 4.71 ms, TE: 2.16 ms, FOV 380 mm,

Matrix: 182 x 320 Slice thickness: 3 mm)

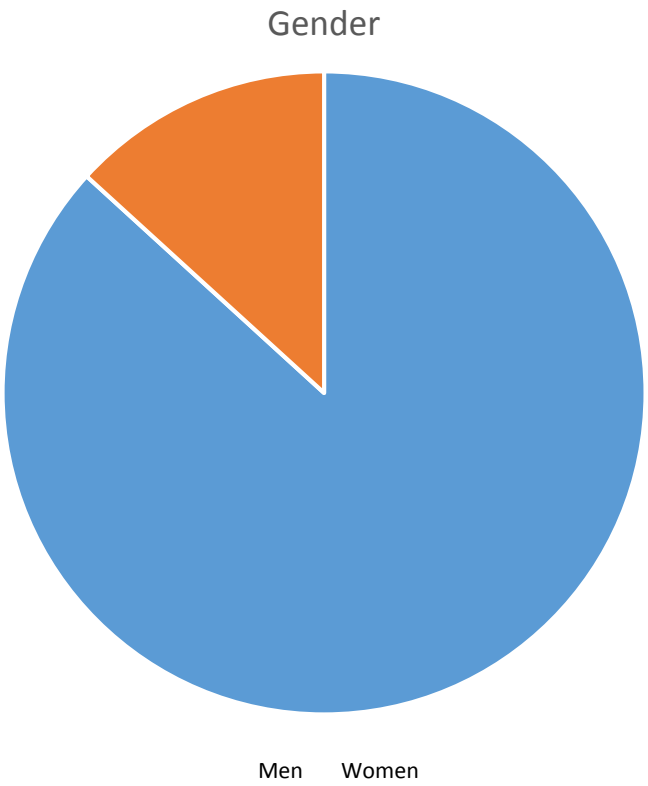
6. DWI, ADC with B-value of 0 and 800

Contrast dosage: IV Inj Dotarem (Gadoteric acid) 0.1 m mol / Kg body weight. ~ 7 ml, followed by ~ 7 ml of normal saline.

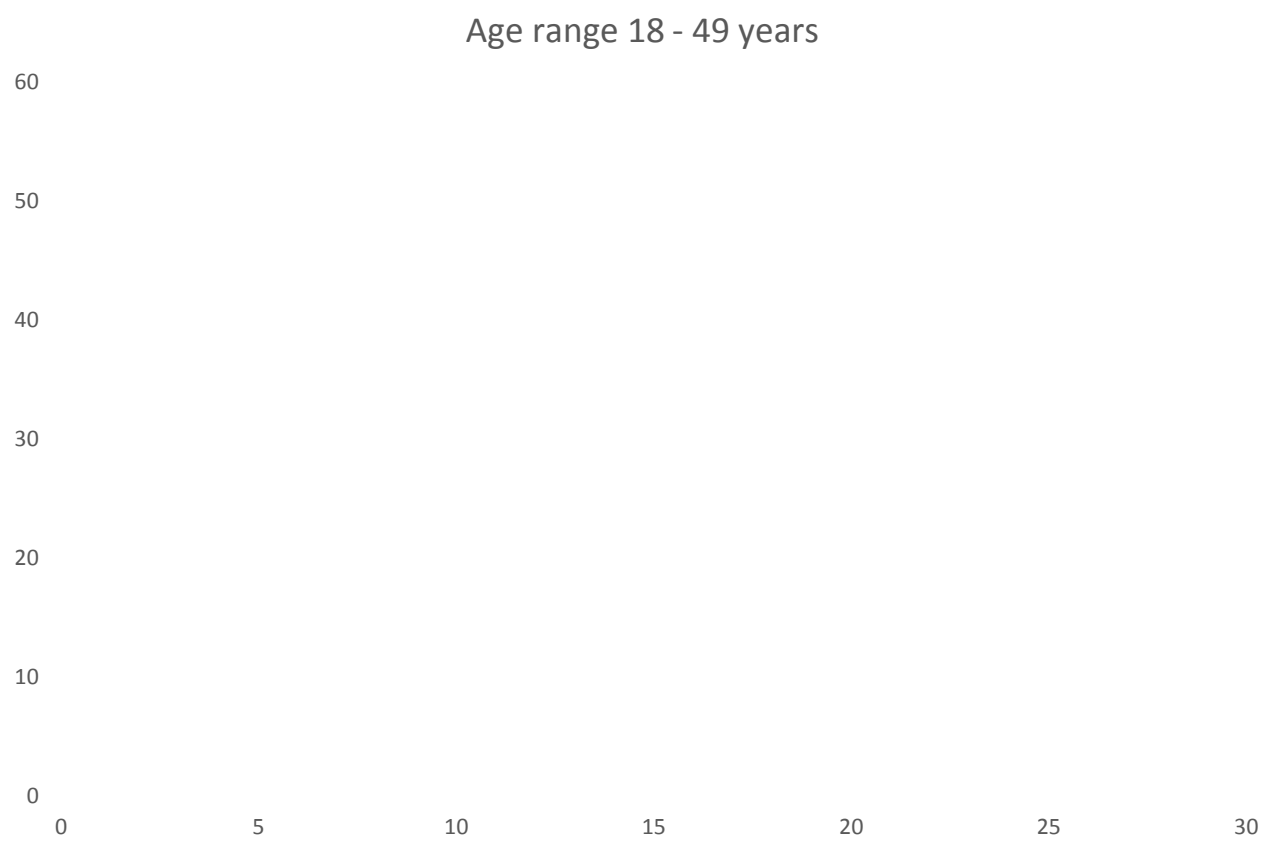
RESULTS:

TOTAL NUMBER OF CASES	25	
NORMAL STUDIES	4	
TOTAL NUMBER OF FINDINGS IN THE ENTIRE SAMPLE	80	
NUMBER OF FINDINGS WITH EXCELLENT AGREEMENT BETWEEN CTE AND MRE	50	62%
NUMBER OF FINDINGS WITH MODERATE AGREEMENT	2	6.6%
NUMBER OF FINDINGS SEEN ONLY ON MRE - NOT SEEN / POOR AGREEMENT WITH CTE	15	53%
NUMBER OF FINDINGS SEEN ONLY ON CTE - NOT SEEN / POOR AGREEMENT WITH MRE	13	46%

Gender: 21 men and 4 women. Total 25



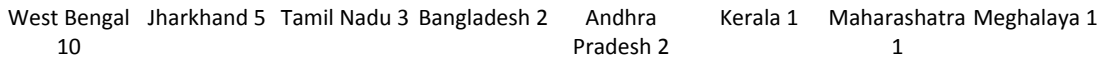
Age: Mean age of the subjects was 32.12 years. Range – 18 to 49 years



Graph depicting the age distribution among the sample

Demography:

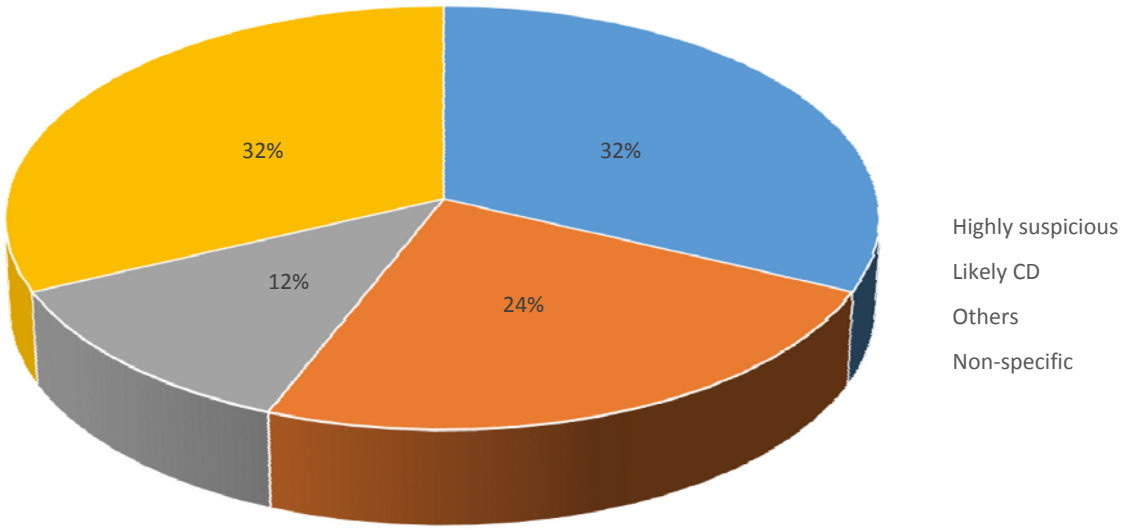
Demographic distribution



Graph depicting the distribution of patients among the states of residence.

Clinical presentation:

Pie diagram showing degree of clinical suspicion for CD. Highly suspicious – almost definitive. Likely – CD is possible but other differentials were also considered. Others- other differentials more likely than CD.



Ileo-colonoscopic findings:

Pie diagram showing degree of suspicion for CD on scopy. Highly suspicious – almost definitive. Likely – CD is possible but other differentials were also considered. Others – polyps, erosions. other differentials more likely than CD.

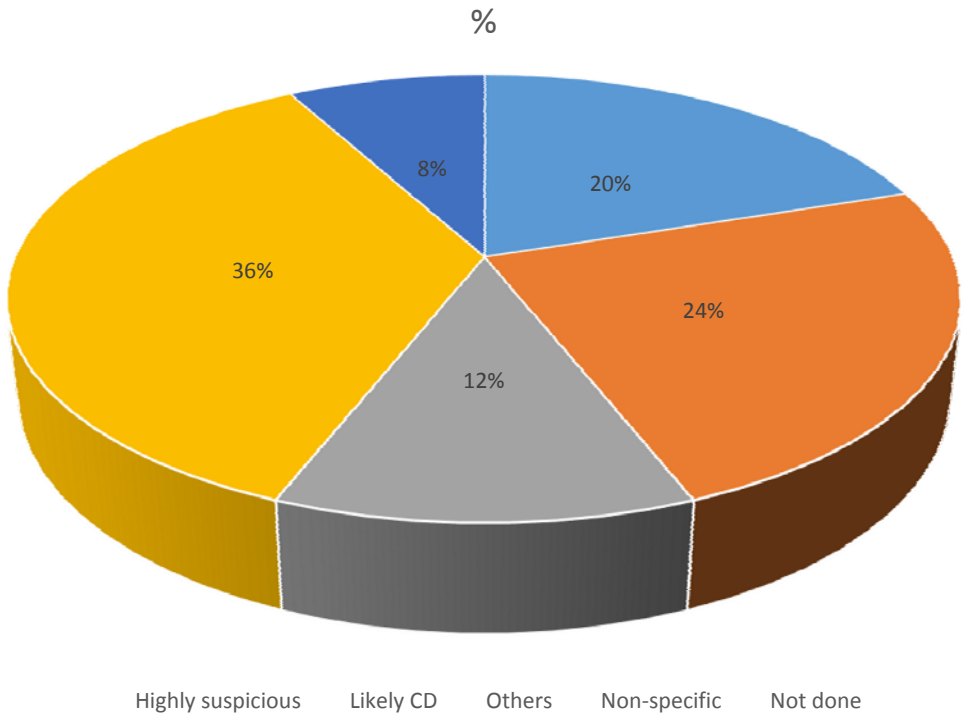
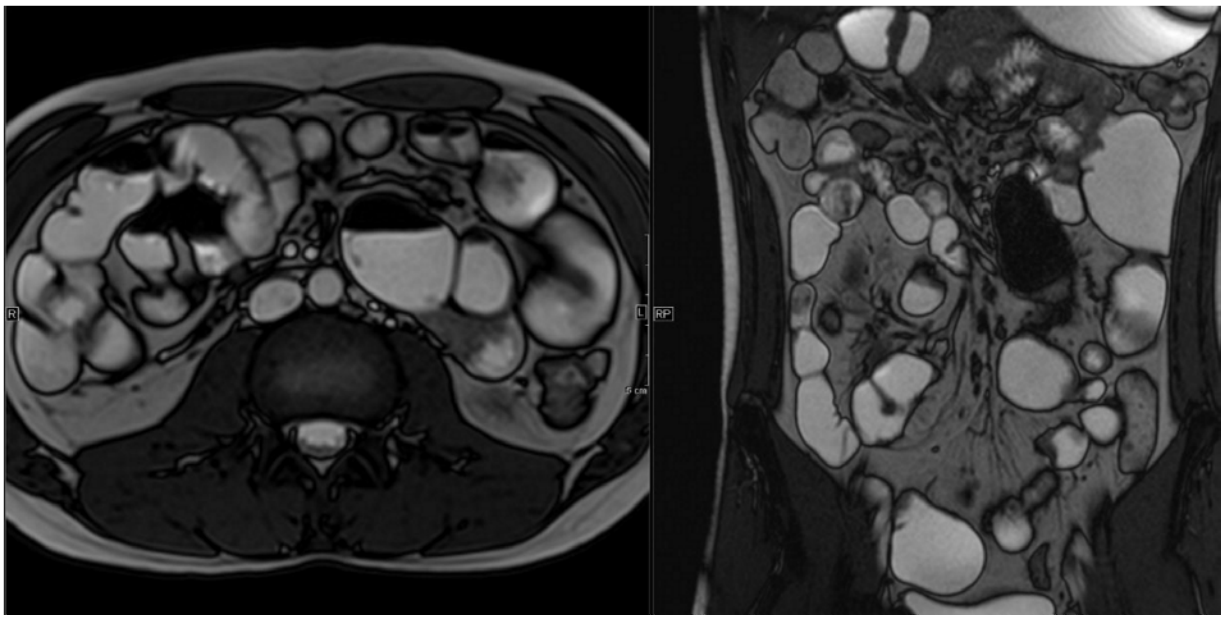


Table showing score for degree of bowel distension (18)

DEGREE OF BOWEL DISTENSION	NUMBER	%
0 – No distension	0	0
1 – Poor	10	40
2 - Good	14	56
3 - Optimal	1	4

Jejunal and ileal axial diameter: Poor - < 20 mm and < 15 mm. Good – 20-30mm and 15-25 mm. Optimal - >30 and > 25 mm



Axial and coronal MRE images showing good bowel distension

Degree of bowel distension:

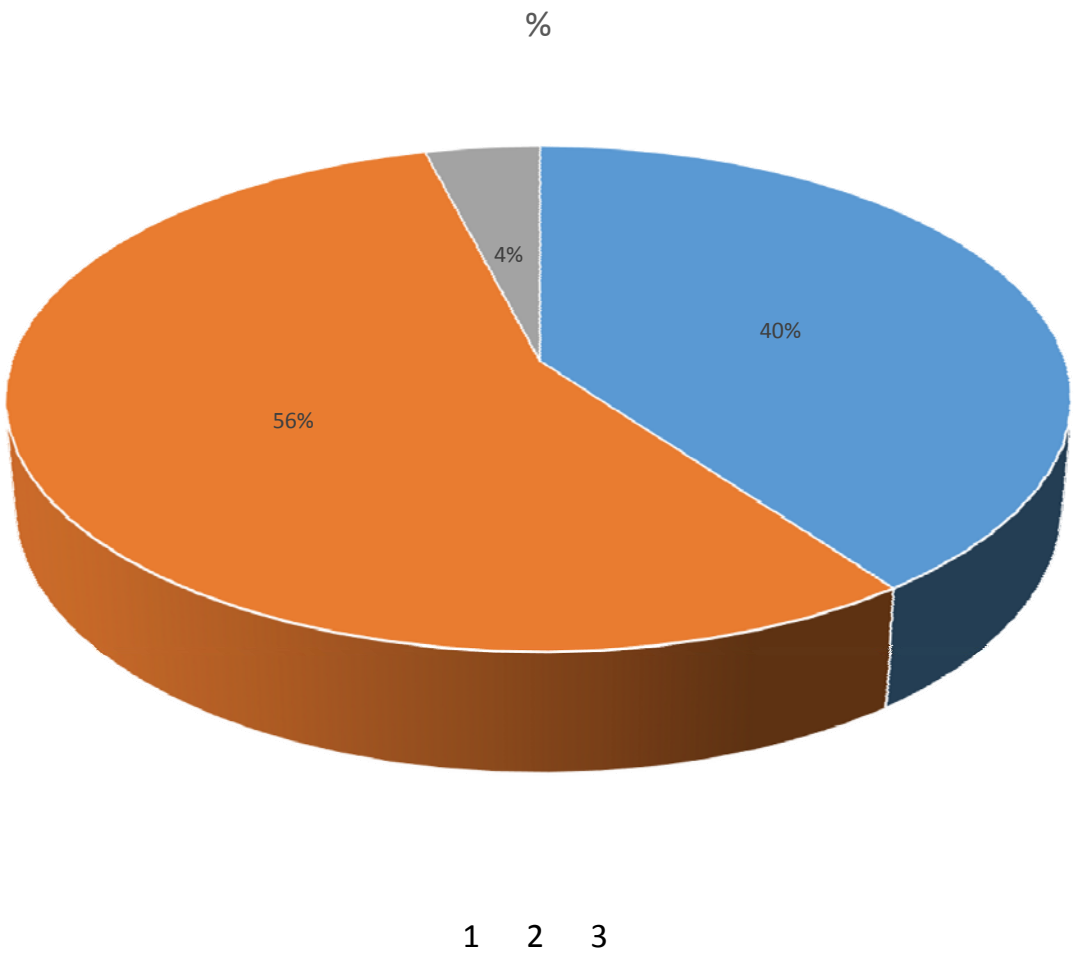
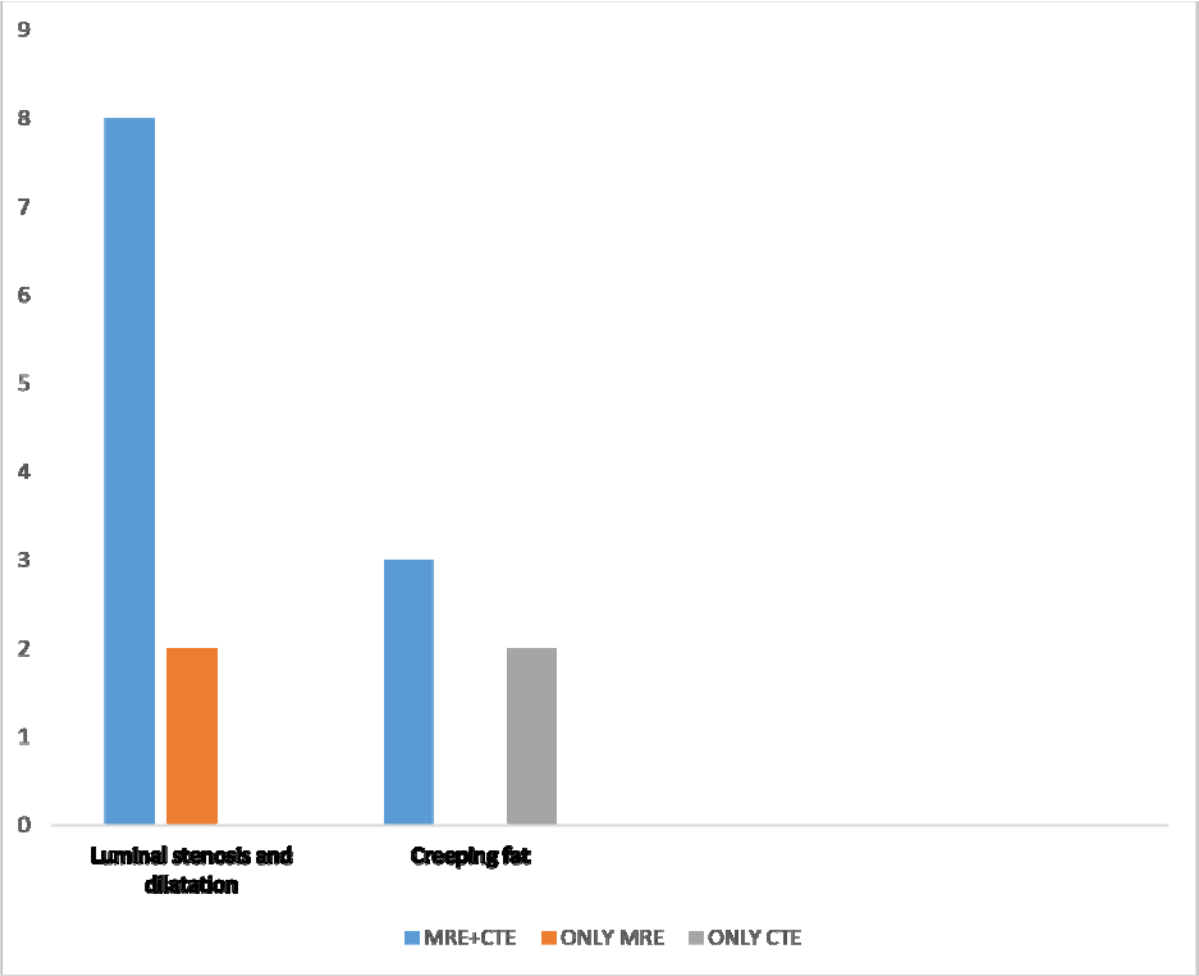


Table showing score for degree of artefacts (18)

DEGREE OF MOTION ARTEFACT	NUMBER	%
0 – No artefacts	1	4
1 – Few artefacts	20	80
2 – Numerous artefacts, but diagnostic images	4	16
3 – Non-diagnostic images	0	0

Bar diagram depicting the diagnostic accuracy of MRE and CTE and MRE+CTE in detecting mural thickening, mural stratification and skip lesions. Vertical axis represents number of patients

Bar chart depicting the diagnostic accuracy of MRE and CTE and MRE+CTE in detecting luminal stenosis and dilatation and creeping fat with or without prominent vasa recta. Vertical axis represents number of patients



The total number of findings in the entire sample of 25 patients were 80.

Four of the studies were normal on both MRE and CTE. Two of these had a high clinical suspicion for CD. Other two had non-specific bowel symptoms. On ileocolonoscopy, one was normal and three had non-specific findings – like superficial ulcers, erosions, mucosal edema and erythema. Biopsy findings of these three patients had non-specific active colitis, with no evidence of CD or TB

Total number of positive findings in combined MRE and CTE in the remaining 24 cases were 80. Among these 80 findings, 50 had excellent agreement between both MRE and CTE (62%). 2 had moderate (not readily visualised / subtle finding) agreement between CTE and MRE (6.6%). One of them was for lymphnode and the other was for creeping fat with vasa recta. Number of findings on MRE that had poor or no agreement with CTE is 15 (out of 28 which is 53%). Number of findings on CTE that had poor or no agreement with MRE is 13 (out of 28 which is 46%). Total number of findings detected on MRE (MRE alone + combined MRE and CTE) is 65 (83% - 65 out of 78). Total number of findings detected on CTE (CTE alone + combined MRE and CTE) is 63 (80% - 63 out of 78).

Table enumerating the above mentioned data:

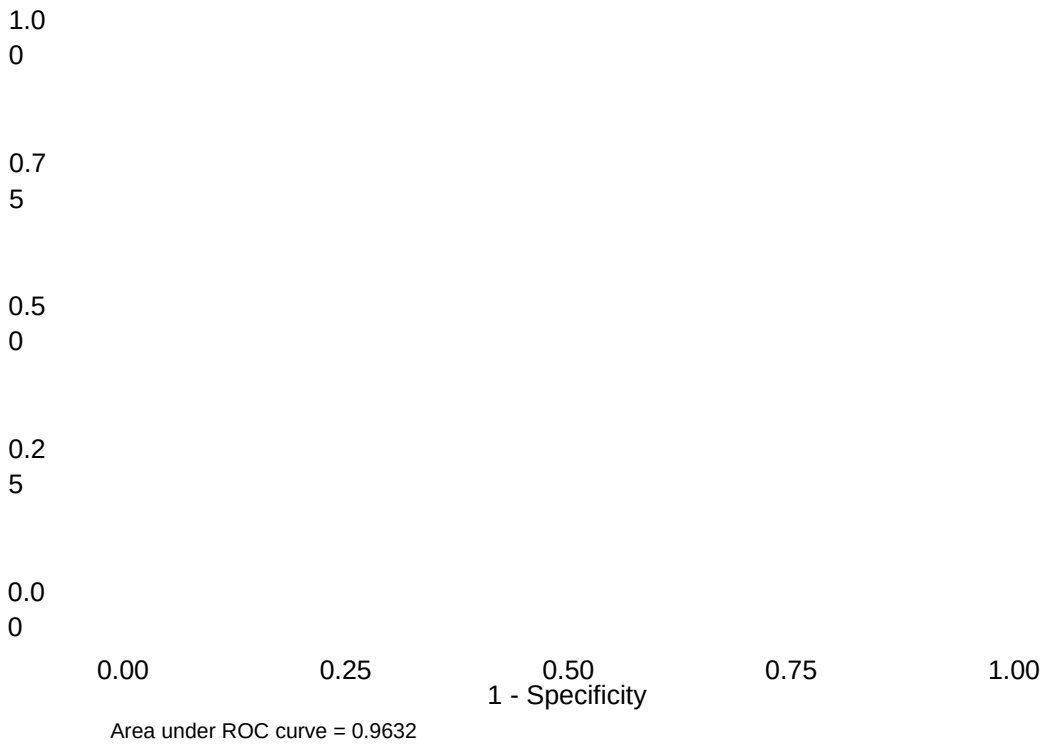
Number of positive cases	24	
Total number of findings	80	
Findings with excellent agreement between MRE and CTE	50	62%
Findings with moderate agreement between MRE and CTE	2	6.6%
MRE findings with poor / no agreement with CTE	15	53%
CTE findings with poor / no agreement with MRE	13	46%
Total CTE findings (alone and combined positive)	63	80%
Total MRE findings (alone and combined positive)	65	83%

Data analysis:

Data analysis was done using statistical analysis method for diagnostic test accuracy. The sensitivity and specificity of MRE in diagnosing CD is 100% and 98.5 % and a PPV of 97.5 % with 95% confidence interval. Agreement between CT and MRI is 52%, Kappa - 0.44 (moderate agreement) and p-value <0.001 which is significant.

Sensitivity	100%
Specificity	98.5%
ROC area – for prev rate of 32, 15 and 53.5%	0.941, 0.862, 1
Likelihood ratio (+)	31.2
Likelihood ratio (-)	0
Odds ratio	10.2
Positive predictive value	95%
Negative predictive value	100%

ROC curve and AUC:



The sensitivity and specificity were calculated with cut-off values for number of findings seen on MRE. Range is from >1 to > 5 findings. The sensitivity for cut-off values of >4 is 100%, > / = 5 is 37.5 %.

Specificity for > / = 3 is 64.7% and >5 is 100%.

The standard error was 0.274. The area under the curve is 0.96, with a confidence interval of 95%.

DISCUSSION:

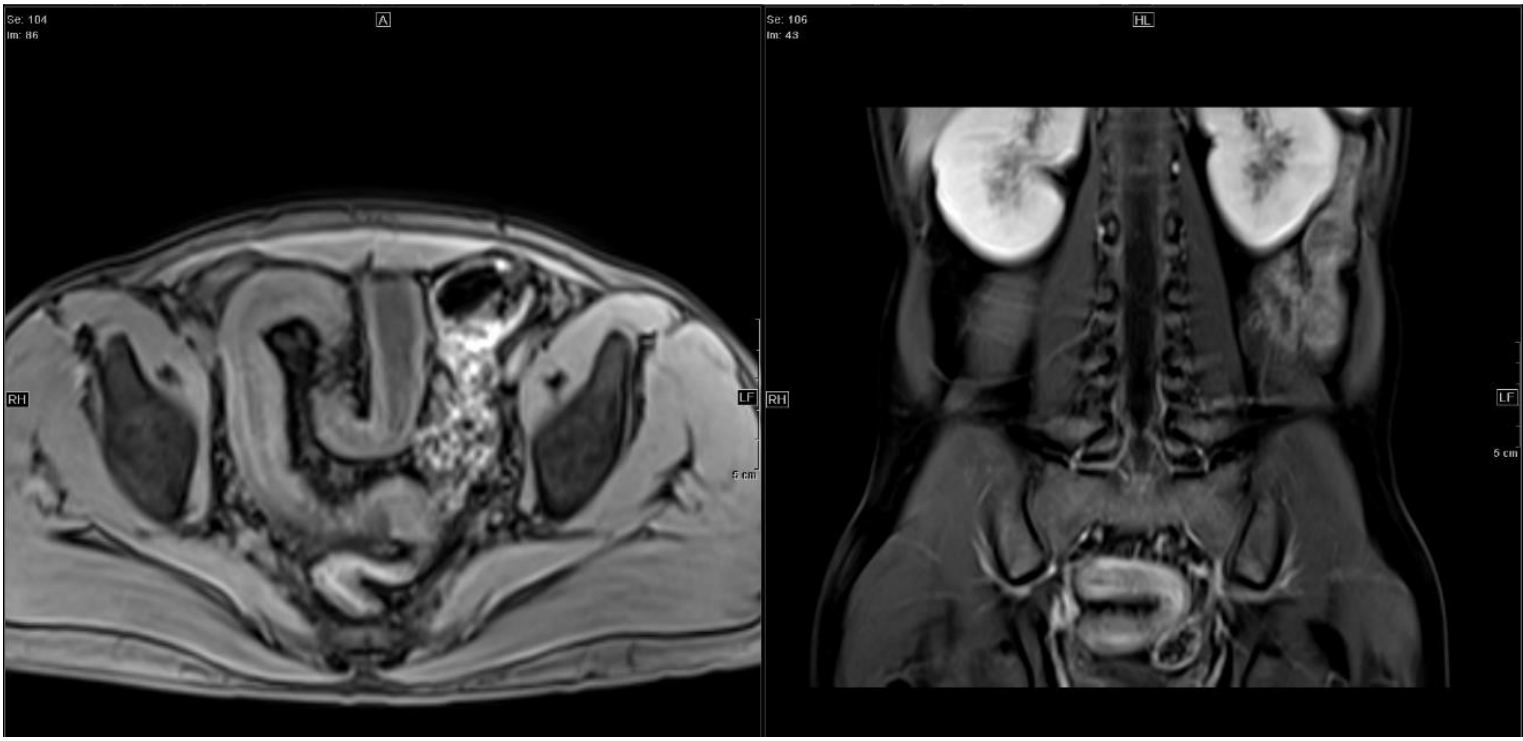
The study consisted of 25 patients, of which 21 were men and 4 were women. The mean age was 32.12 years. Demographic distribution of the sample was among West Bengal (10), Jharkhand (5), Tamil Nadu (3), Bangladesh and Andhra Pradesh (2 each), Kerala, Maharashtra and Meghalaya (1 each).

As described in the methodology, all patients were either proven cases of Crohn's disease or with a high suspicion for the same. They were scheduled for a routine CTE by their gastroenterologist. On the same day MR Enterography was also performed with consent, prior to CT. Since MRE and CTE were done on the same day, taking oral contrast twice for 2 tests was avoided. There were no complications during either of these studies. All patients tolerated the tests well and showed good compliance with regards to consumption of oral contrast and breath-hold during the tests.

Variables:

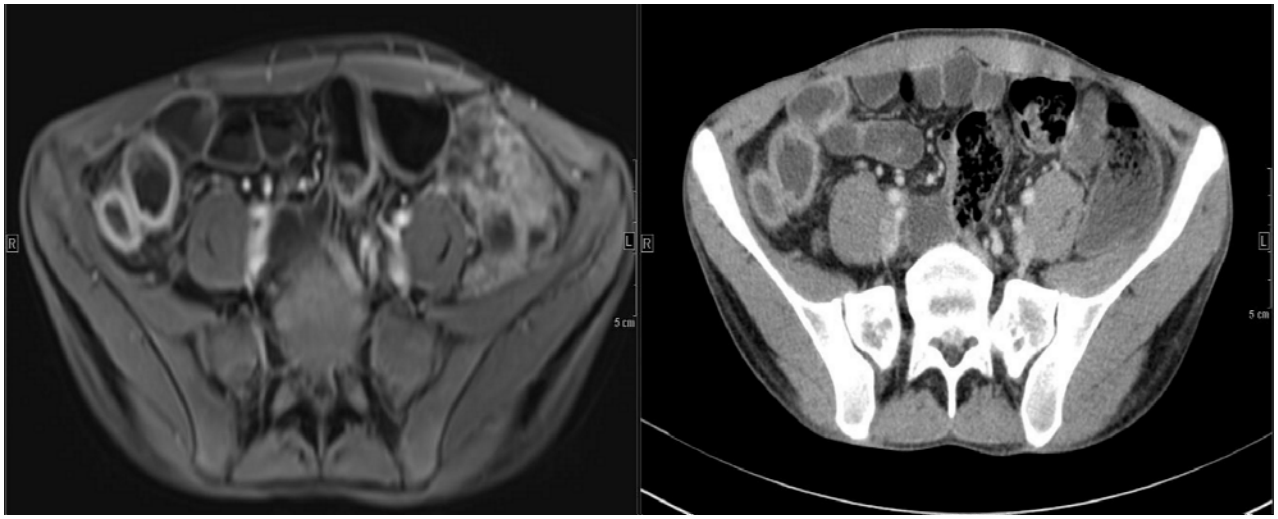
General variables studied were age, gender, degree of bowel distension, artefacts score, clinical presentation, scopy findings and biopsy findings.

Variables specific for CD were mural thickening, stratification, skip lesions, luminal stenosis, luminal dilatation, phlegmon, abscess, fistula, creeping fat and lymphadenopathy. For the 5 mural findings, segment of bowel involved were also assessed on CT and MR. For the extra-mural findings – its presence or absence and their location was studied.



Mural thickening:

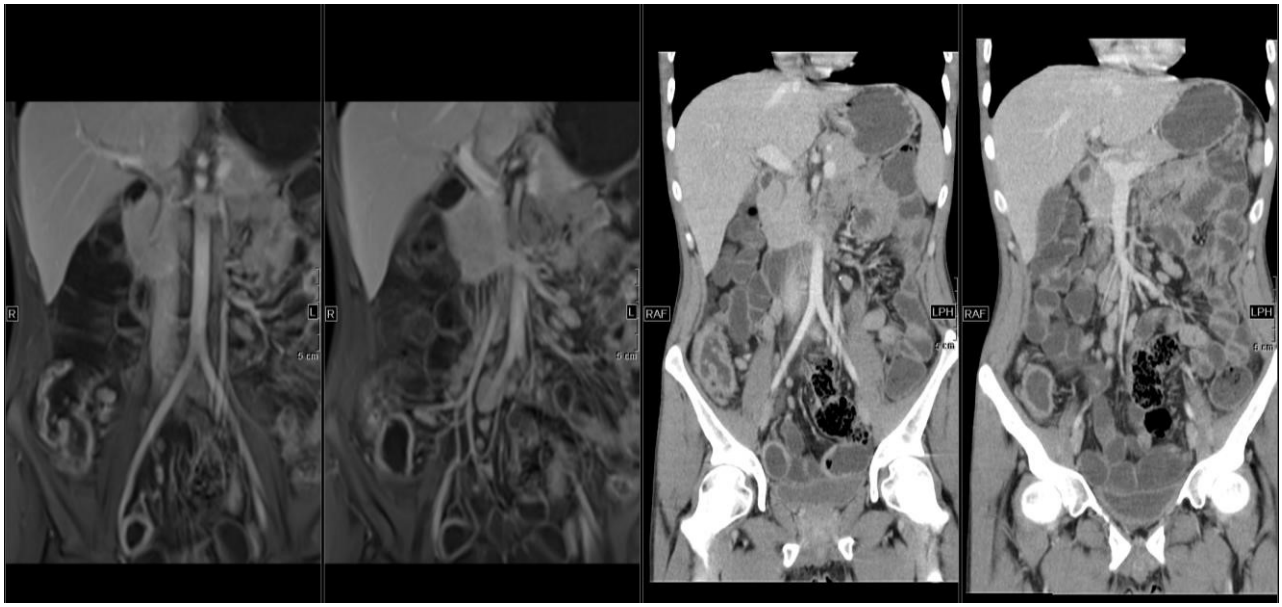
T1 post contrast axial and coronal MRE image showing long segment mural thickening with stratification in sigmoid colon



Mural thickening without stratification

Axial T1 VIBE post-contrast and CTE venous phase

This is the most common finding seen in the overall sample (excluding the 4 normal studies) seen in all 21 patients (100%). In two patients with mural thickening seen in low rectum and distal jejunum / proximal ileum, the finding was better seen on CTE than MRE. Short segment of disease and different slice thickness between the two modalities (MRE 5 mm, CTE 3 mm) are the likely cause for this. Only small bowel is involved in 8 patients and large bowel only in 10 patients. Both small and large bowel were involved in the remaining 3 patients. Most common segment involved is the recto-sigmoid colon, followed by terminal ileum



T1 post contrast coronal MRE images and coronal CTE images in venous phase, showing mural thickening in IC junction and skip lesion in distal ileum

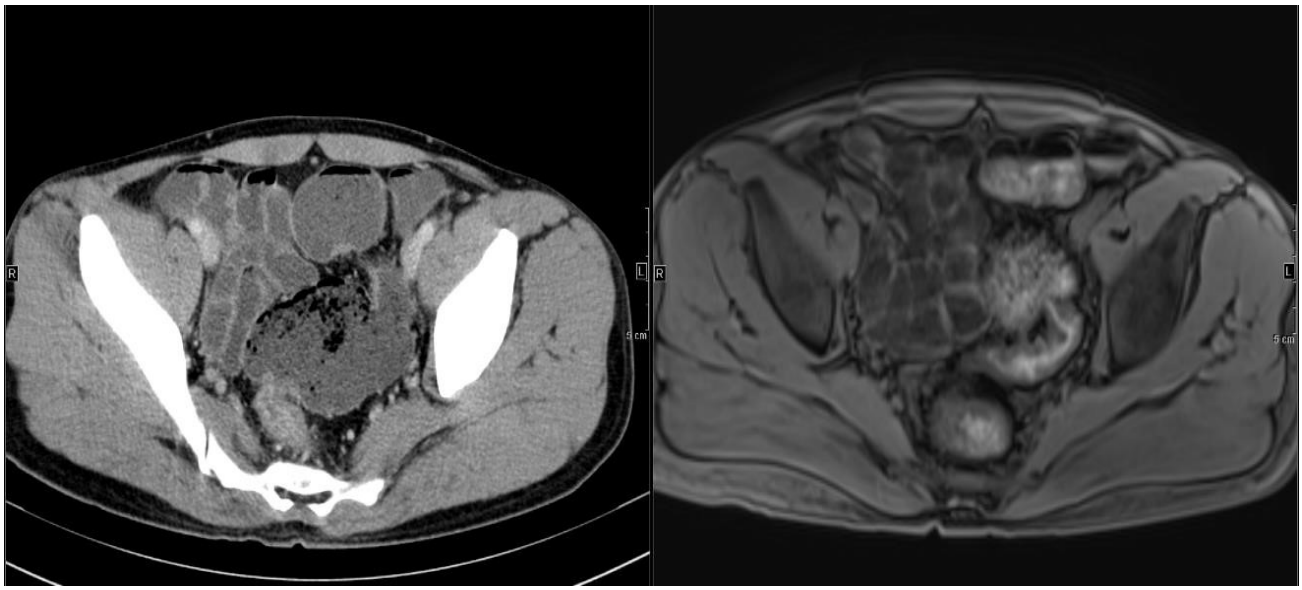
Stratification:

Mural stratification is the next common finding, seen in up to 12 out of the 21 patients who showed mural thickening (57%). This finding is seen in both MRE and CTE in 3 patients only. In 9 out of the 12 patients with mural stratification, the finding is seen only on MRE (75%). Therefore MRE has 100% accuracy in detecting mural stratification compared to CTE which is 25%. These results were similar to the study done by Amitai et al (15)

Skip lesions:

These were seen in 8 out of 21 patients (38%). Both MRE and CTE showed excellent agreement in detecting skip lesions. 30% were seen in small bowel and 70% in large bowel

Luminal dilatation and stenosis:

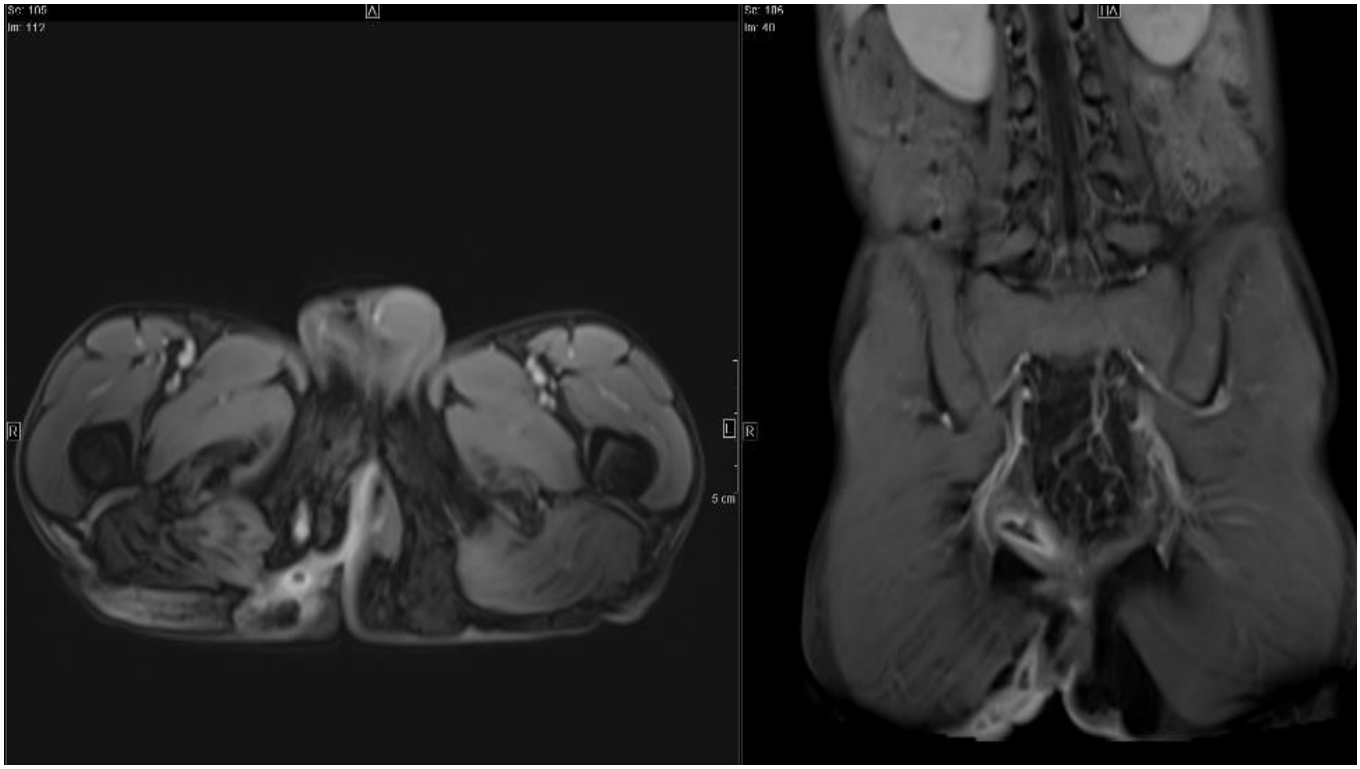


Axial CTE and MRE T1 VIBE pre-contrast image showing luminal stenosis, with proximal dilatation

Since these two findings were seen in contiguous segments, they were analysed together. 8 out of 21 patients had 10 segments (47.6%) of luminal stenosis and dilatation. All were short segment disease, with no bowel obstruction. Of the 10 segments, 8 were seen in both MRE and CTE while 2 were seen only on MRE.

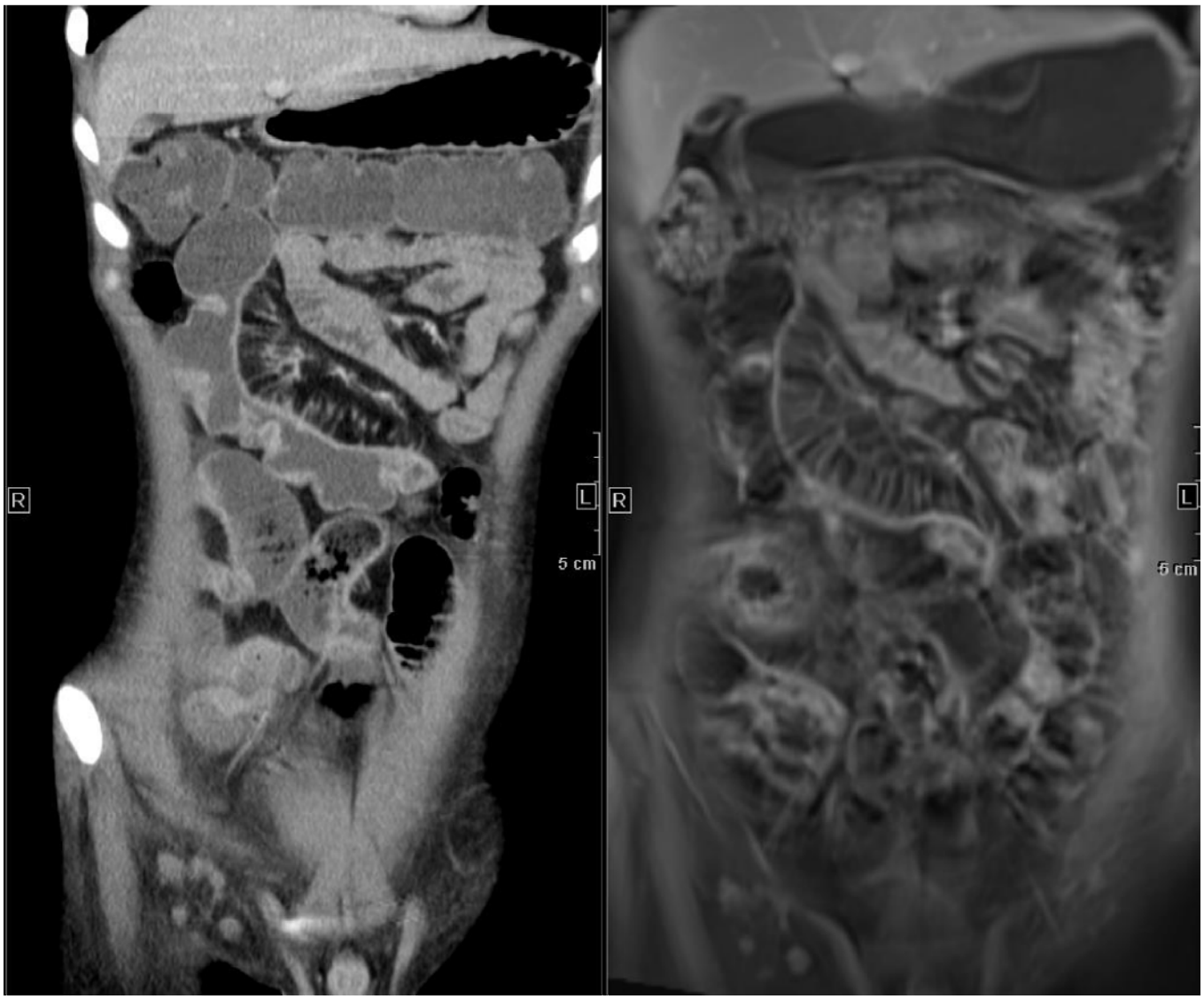
Overall MRE had 100% accuracy in detecting this findings compared to 80% on CTE.

Fistula:



This finding was seen in 4 patients. All had perianal disease. Both CTE and MRE were equally accurate in detecting this finding.

Creeping fat:



Creeping fat with prominent vasa recta on CTE venous phase coronal image and T1 VIBE post-contrast coronal image

This indicates fatty deposition along the mesenteric border of inflamed bowel loop.

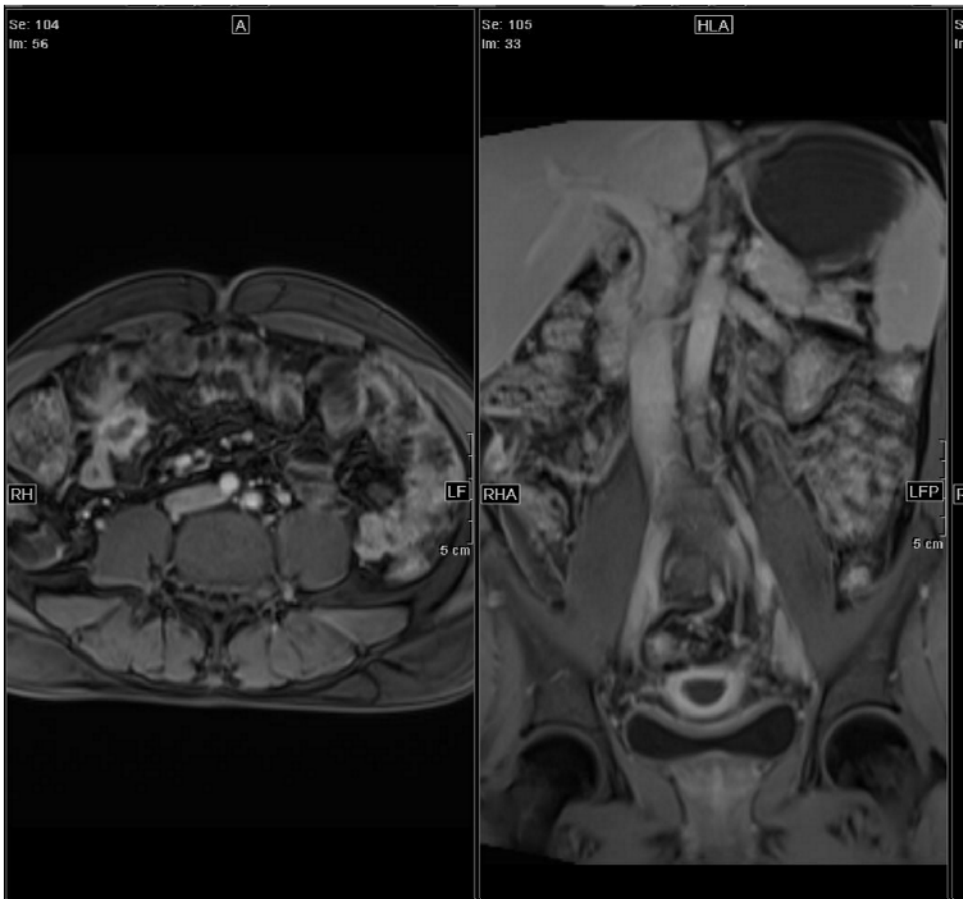
(15). This finding was seen either in isolation or with prominent vasa recta – indicating

active inflammation. It was present in 6 patients. Out of which MRE could detect only 4 (66%), while CTE showed 100% accuracy – especially with prominent vasa recta. The reason for higher accuracy with CTE is attributed to the timing of contrast injection – which is dynamic on CTE through pressure injector and slightly delayed by about 10 – 15 seconds as Gadolinium was injected manually and then scan was resumed. However, in the studies done by Amitai et al and Jensen et al, they have shown than both studies had excellent agreement and MRE had higher diagnostic accuracy to detect creeping fat sign. (15, 16).

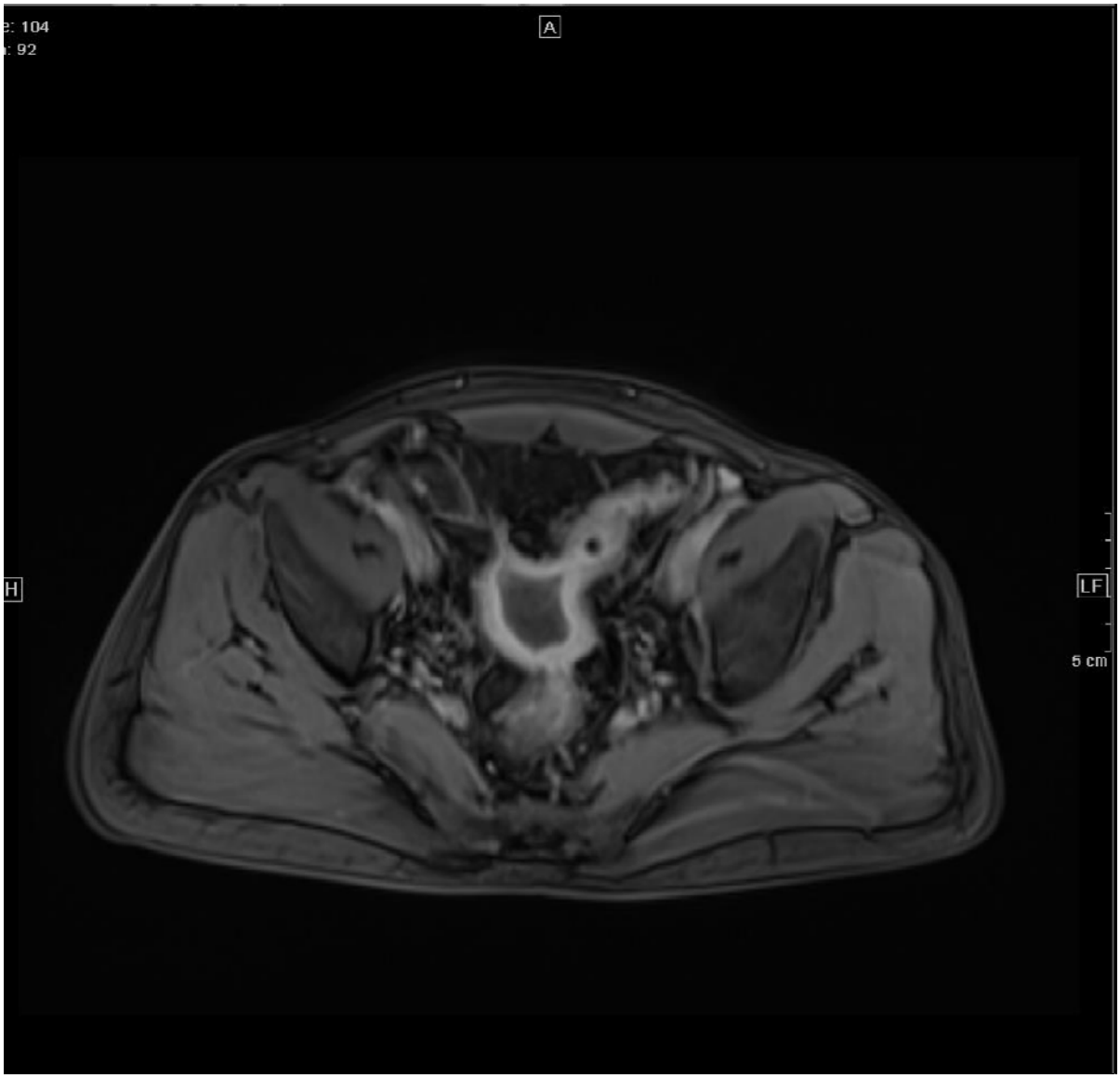
Abscess:

Perianal abscess

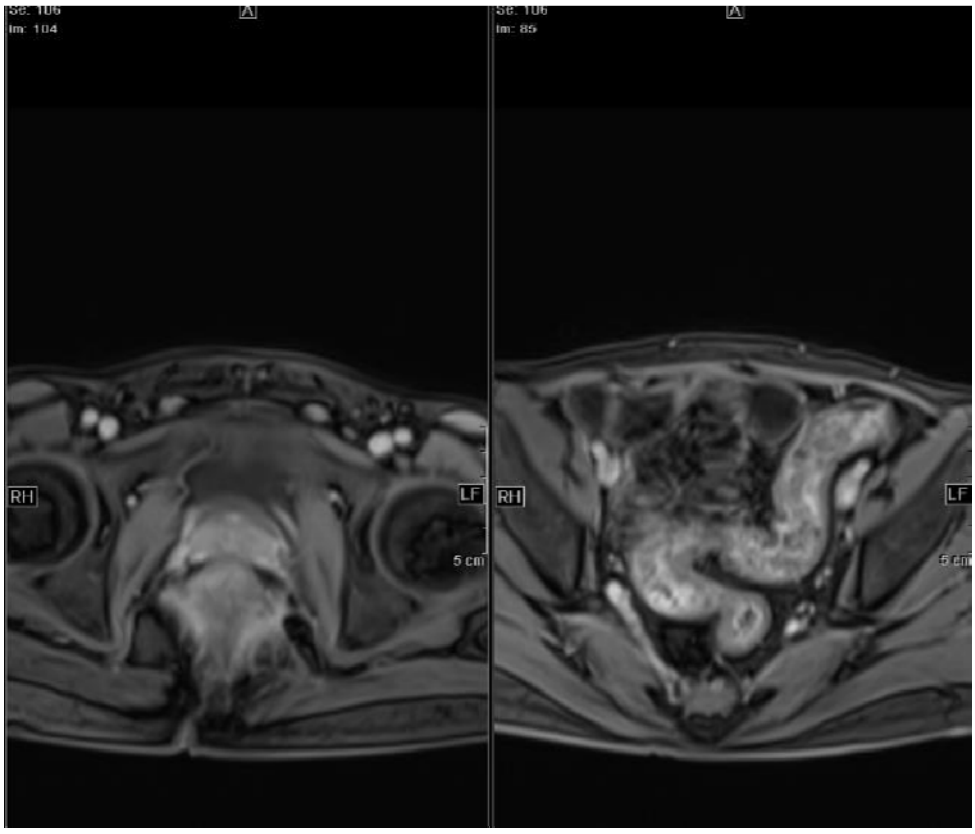
Abscess was seen in 4 patients. 3 of which were associated with perianal fistula. 1 had an interloop abscess, which was better seen on CTE than MRE.

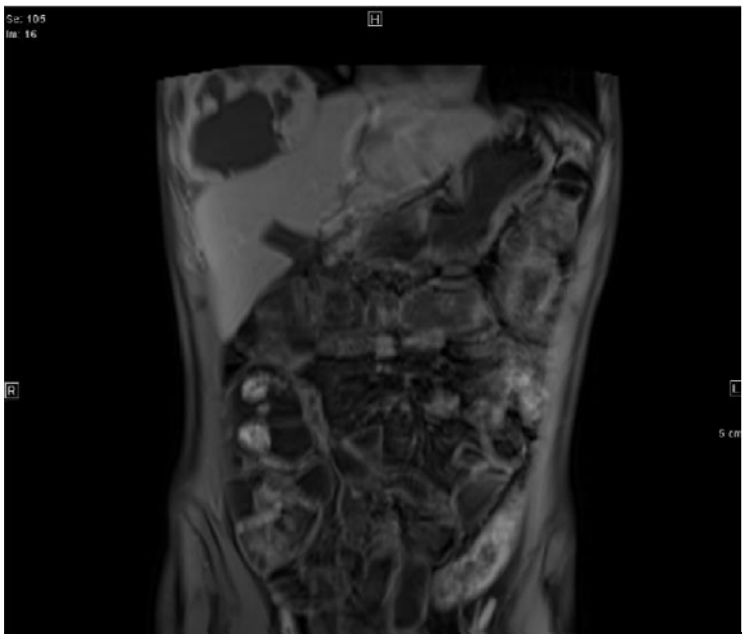


Interloop abscess

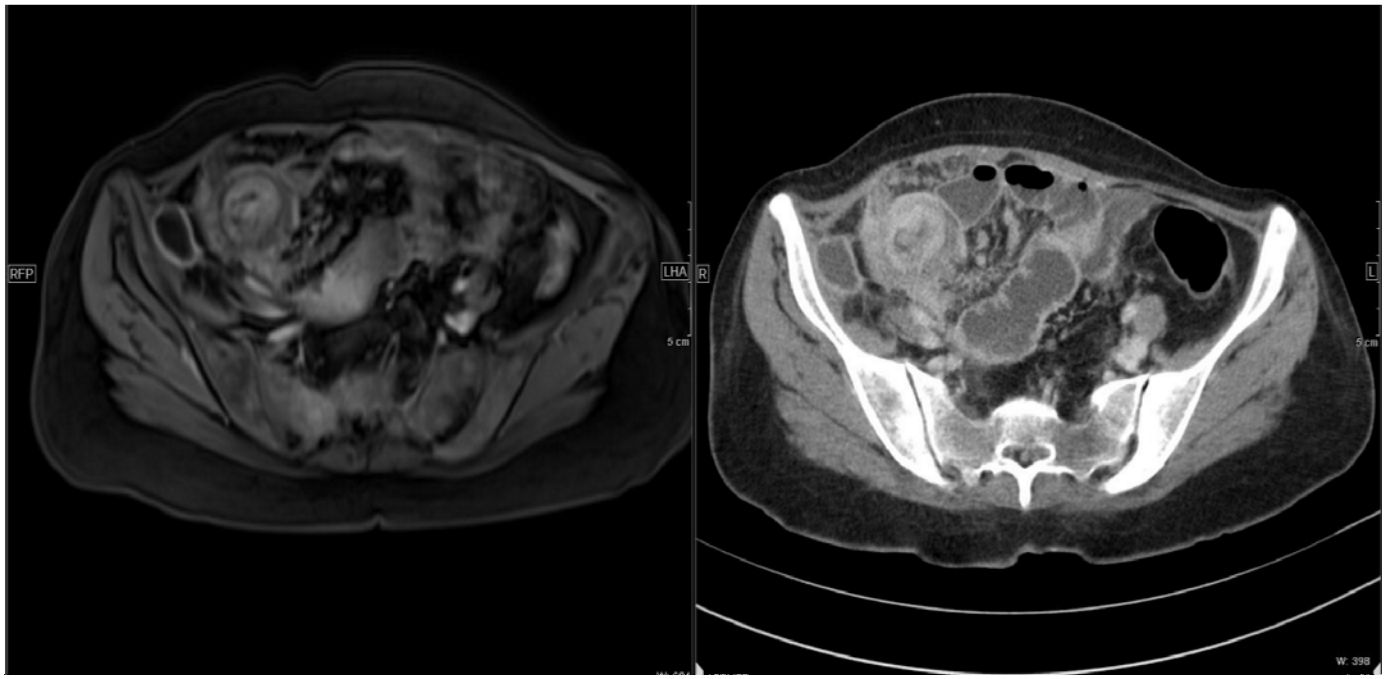


Interloop abscess





Right subdiaphragmatic abscess. Long segment rectosigmoid involvement of disease



Lymphadenopathy:

Necrotic node with enhancing walls in right iliacus muscle

Present in 6 patients. All measuring 9-10 mm in short axis diameter. 4 had agreeable results while in 2 there was moderate agreement - CTE was able to detect readily and not on MRE. These were likely to be reactive nodes and there were no regional bowel disease. These were similar to the results obtained by Amitai et al. (15)

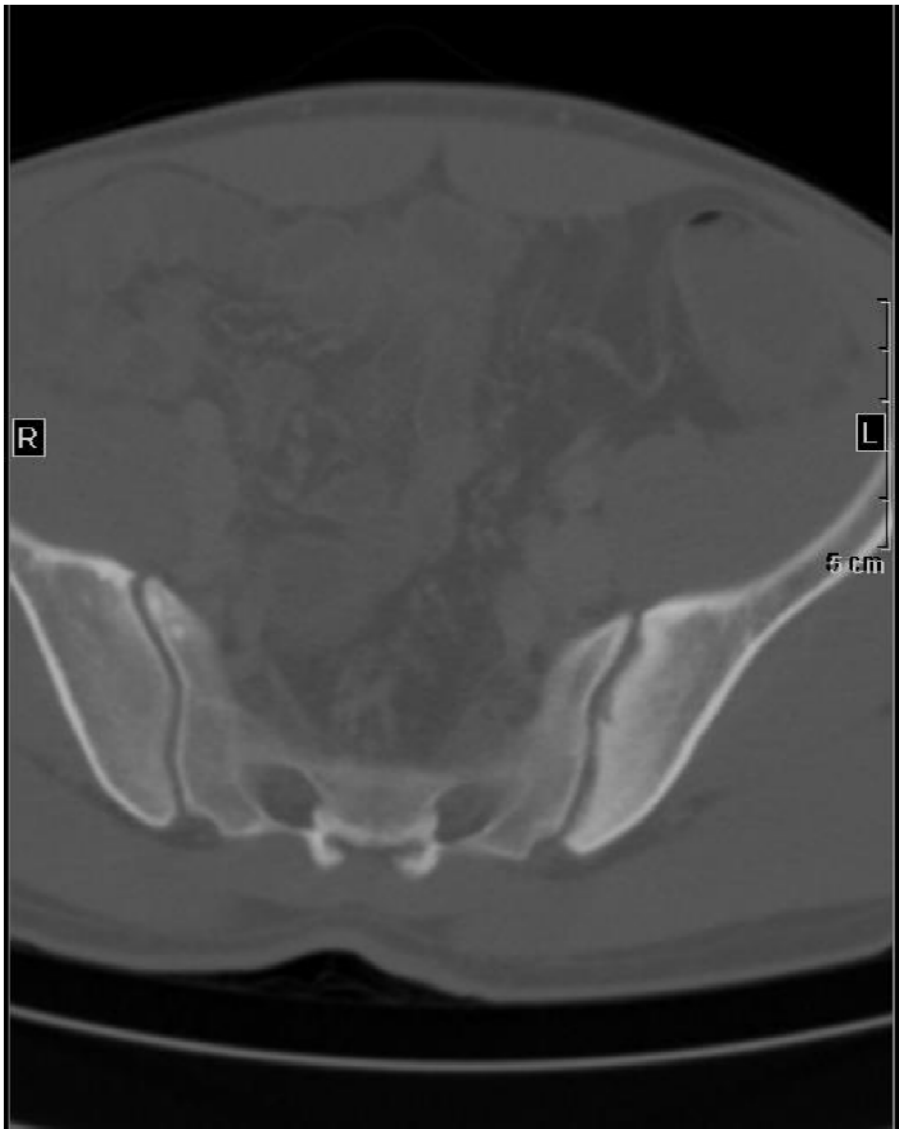
Phlegmon: No patient had significant phlegmon

Other observations:

- One patient had minimal free fluid in the pelvis, which was detected easily on CTE while not on MRE. Likely due to the difference in the degree of regional bowel distension seen between the two tests, which alters the distribution of the fluid in the interloop spaces.

- Two patients had sacroiliitis, that were detected on CTE, which had better diagnostic

accuracy than MRE. Dedicated MRI sequences may be required to assess these.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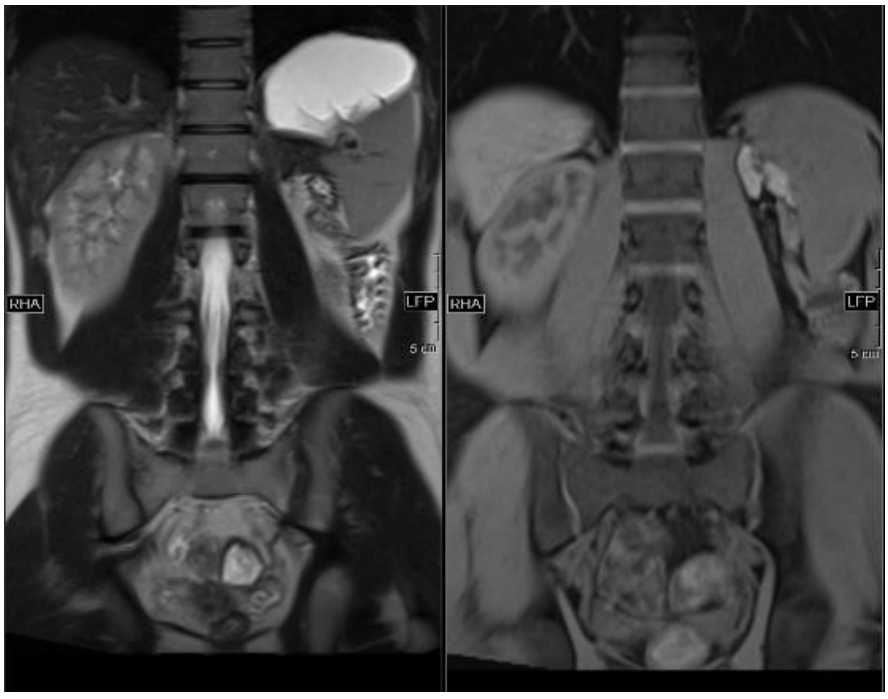
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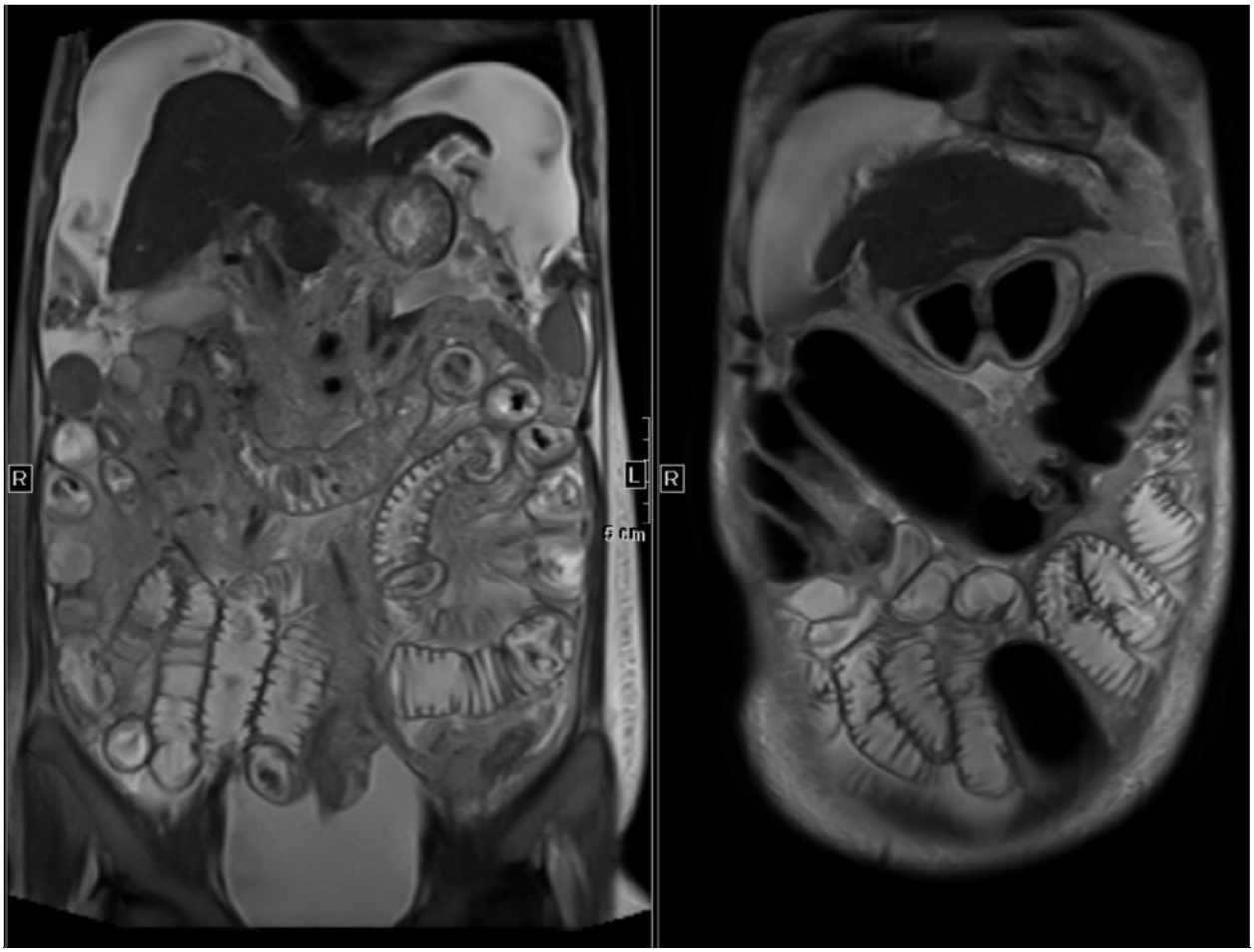
RHA
LFP

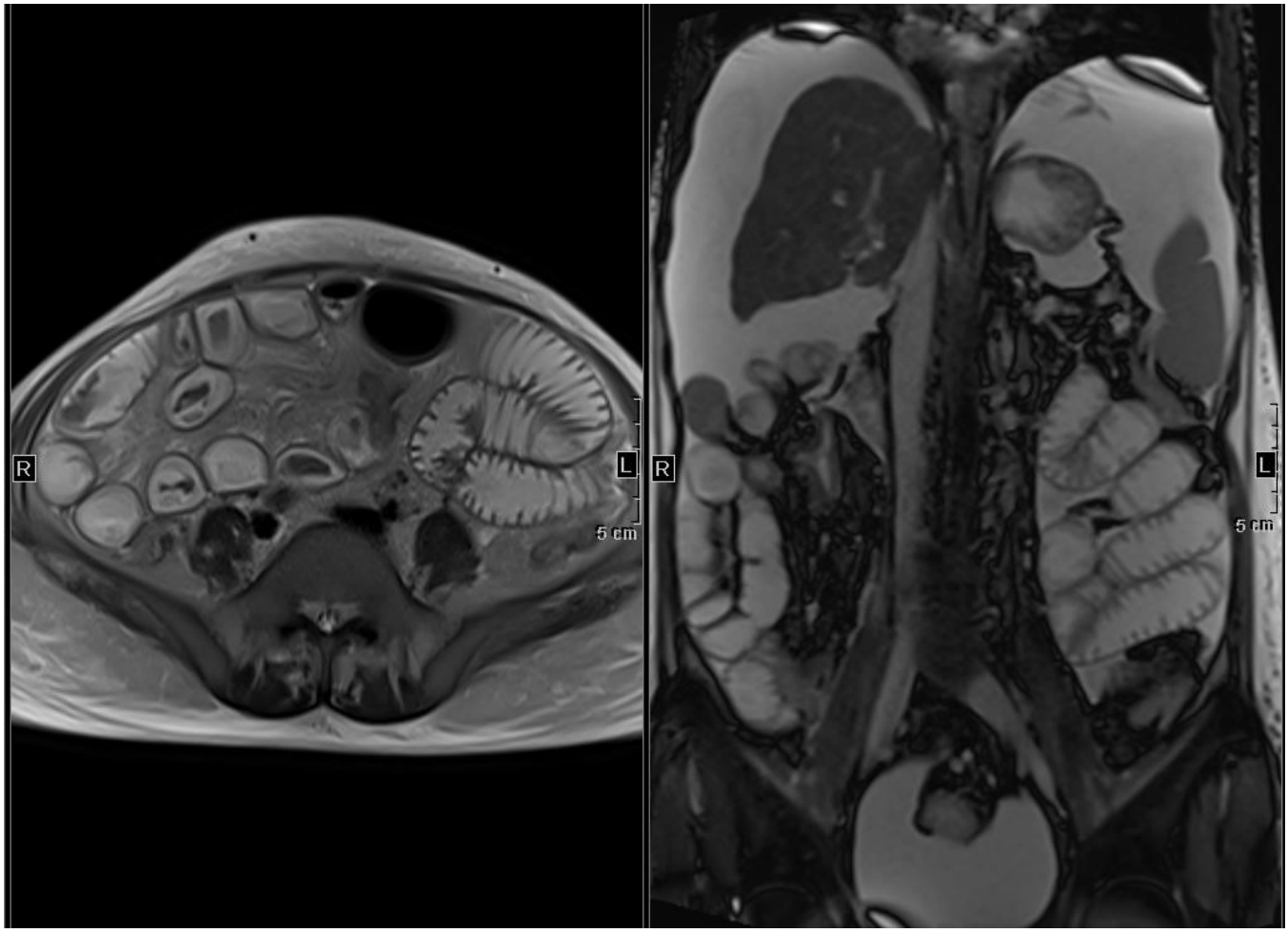
This patient was found to have left sacro-iliitis detected on CTE. This finding was not readily seen on MRE.

However, dedicated sequences like T2 SPAIR and T1 coronal were more sensitive

- A patient with co-existing chronic liver disease and ascites showed good anatomical details of the small bowel on both CTE and MRE. This is due to better spatial resolution and better inherent contrast between ascites and bowel wall.



A patient with co-existing CLD and ascites we found that anatomical details of the bowel wall are well appreciated on both CTE and MRE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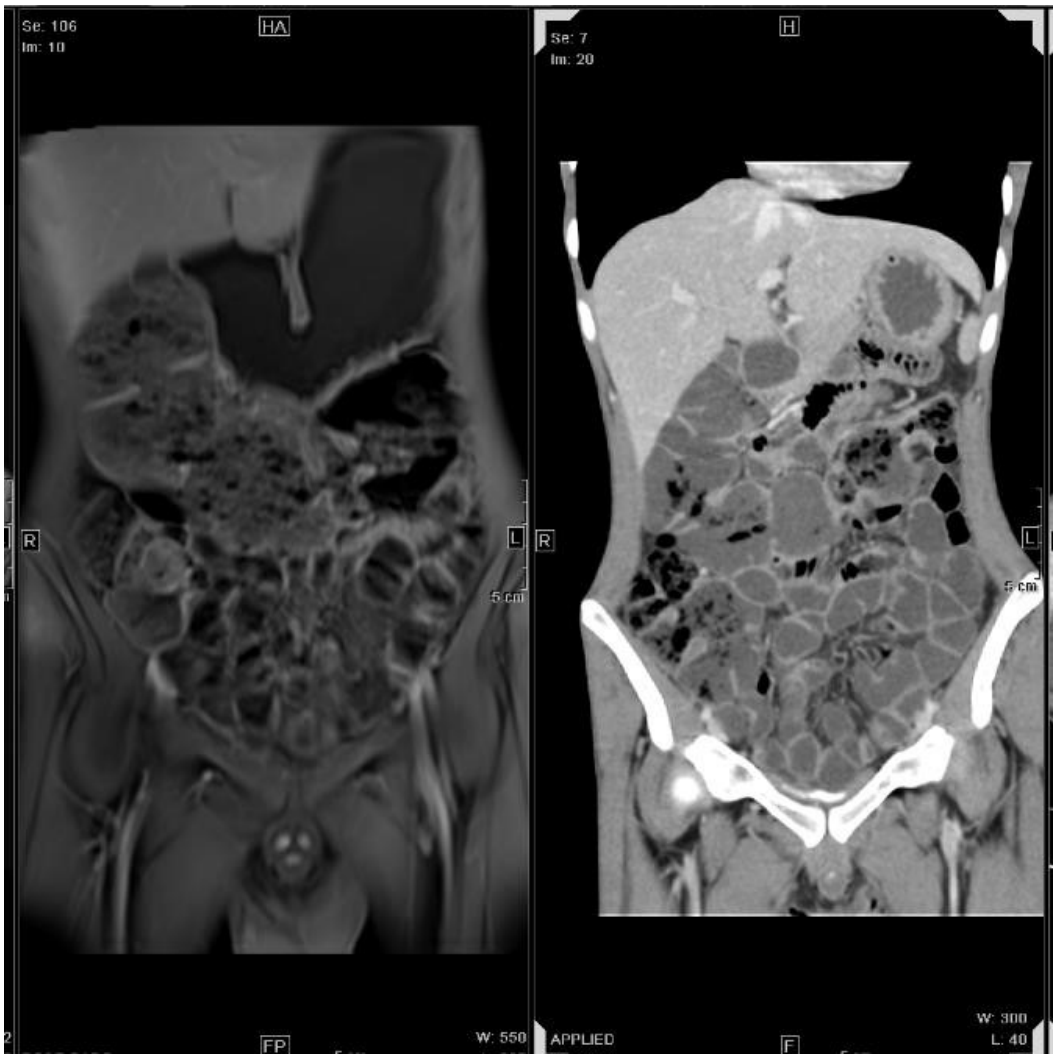
- Patients with moderate to severe disease involving the rectum and anorectal region had proximal loaded colon, detected on both CTE and MRE. However, this did not affect the image interpretation



Limitations:

1. There is no similar study in the Indian population for comparison. Since environmental cause plays a significant role in CD, the natural history is different in the Indian subjects. Genetic cause like NOD2 gene mutation identified in the Western population with CD is not seen in the Indian population.

2. Sample size as calculated could not be met due to limitations of time availability. Further recruitment for this study is ongoing.

3. Most patients had only average score for degree of bowel distension on MR compared to CT. Though it did not affect the outcome, it is suboptimal for enterography technique.

4. DWI were not evaluated in detail at present, due to scanty reference articles. However, the data was obtained and will be analysed later. Cine coronal HASTE described in literature to detect early motility changes in the affected loop was not included in the protocol. However, this did not affect the outcome, since apparent stenosis seen in one sequence is looked for in other sequences, before diagnosing it as stenosis.

Overall comparison of our study with the study done by Amitai et al, published in May 2015 in IMAJ (15). Agreement between CTE and MRE for the findings in

Crohn's disease

FEATURE	**RESULTS FROM OUR STUDY N=21**	**RESULTS FROM OUR REFERENCE STUDY. N=42**
Mural thickening	17 / 21	38
Mural stratification	7 / 7	33
Skip lesions	8 / 8	34
Stricture and dilatation	10 / 10	36
Creeping fat	3/5	30
Fistula	3/4	33
Abscess	3/4	31
Adenopathy	3/6	23

Our study result numbers indicate the ability of MRE to detect each finding compared to combined ability of CTE and MRE. For example, 17 /21 means, the combined (CTE + MRE) positive for mural thickening is 21, of which 17 were detected on MRE alone or combined and in 4 cases, MRE could not detect the finding.

Summary of the table:

Compared to the reference study quoted, mural thickening, stratification, skip lesions and luminal stenosis had high degree of agreement between MRE and CTE. Adenopathy and creeping fat showed low agreement. Our results were similar and comparable with the reference article, on which our study is based

Conclusion:

1. In this study we found that the overall sensitivity, specificity and PPV of MRE in detecting the 10 mural and extramural findings are 100%, 98.5% and 95%. It was compared with the standard imaging test – CTE. Overall there was moderate agreement between the two diagnostic tests with a Kappa of 0.4. MRE alone had a diagnostic accuracy of 83%, compared to CTE, which had 80% accuracy. Therefore MRE is an excellent radiation-free diagnostic test in the evaluation of CD.

2. In our study, MRE showed 66% accuracy in detecting creeping fat, compared to CTE which is 100%. The reference articles have reported better diagnostic accuracy on MRE for this finding. Similar studies by Amitai et al and Jensen et al, also showed excellent agreement for 8 out of 10 signs and poor agreement for atleast 2 signs. Also, since creeping fat is seen along the mesenteric border of the inflamed bowel loop, this finding does not occur in isolation (15)

3. Single-most sequence that is most diagnostic on MRE was post contrast T1 sequence in axial and coronal planes.

4. Mural stratification, which indicates transmural inflammation is a hallmark of CD. In our study we found that MRE has 100% accuracy in detecting mural stratification compared to CTE which is 25%.

5. Patients with fistulising disease – mainly perianal disease was present in our study. They need additional imaging with high resolution MRI sections through the pelvis for a comprehensive evaluation.

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Appendix 1: Patient information sheet

DEPARTMENT OF RADIOLOGY, CHRISTIAN MEDICAL COLLEGE, VELLORE

PATIENT INFORMATION SHEET

Study Title: Comparison of MR enterography & CT enterography in patients with Crohn's disease

You are requested to participate in a study which compares the disease status on CT scan and MRI scan. By using MRI, more details can be identified, without the harmful effects of ionizing radiation used in CT

What is MR enterography (MRE)? How is it different from CT enterography?

MRE is a test to assess the small digestive system, especially the small bowel – which is frequently affected in Crohn's disease.

The type of the scanner is slightly different. A different injection (dye) is given during the scan and the scan takes longer time than CT scan

Does MRE have any side effects?

No. There is no exposure to ionizing radiation or other side effects.

If you take part what will you have to do?

If you agree to participate in this study, on the day of the CT scan, which is already scheduled for you, MRE will be done first, then CT scan will be done. You will be asked to drink a solution (peglec mixed in water) for the CT scan. After 45 minutes, MRI scan will be done. During the scan, two injections will be given – Buscopan to decrease the bowel movements & contrast. The scan will take about half an hour. After that CT scan will be performed as scheduled. Both the scans will be reported by radiology doctors. Treatment will be planned based on reports.

There will be no change in other investigations advised by your doctor. No special blood test will be required for this study.

Will you have to pay for the MRI scan?

No, you will not be charged for the MRI scan. All other investigations will continue in the usual manner as advised by your doctor.

What happens after the study is over?

You may benefit from the study, if MRI scan shows findings not seen on CT scan. If there are no new findings on MRI, compared to CT, then there is no benefit. However, this will not affect the treatment plan. The final results of this study will interpreted at the end of 8 months. If we come to a conclusion that the study is beneficial, we will be able to use the information in assessing patients with similar conditions in future. Also the scan will be standardised to suit our patients, so that it is cost effective & less time consuming.

Will your personal details be kept confidential?

The results of this study may be published in a medical journal but your identity will not be revealed in any manner. However, the images may be reviewed by other specialists associated with the study without your additional permission.

If you have understood the information about this study, and if you are willing to voluntarily participate in this study, we can do the MRI scan.
During the scan, if you feel uncomfortable and if you do not want to complete the scan, you can withdraw from the study

If you have any further questions, please contact Dr Bernice TS (Ph. 0416 307 3012) or E-mail: bernice.devarajan@yahoo.com

Appendix 2: Patient consent form

CONSENT TO TAKE PART IN STUDY

Study Title: Comparison of MR enterography & CT enterography in patients with Crohn's disease

Study Number: _____

Participant's Name: _____

Father's/Husband's Name: _____

Age: _____ Sex: Male / Female

Hospital No.: _____

I declare the following: (please tick the boxes)

(i) I have read and understood the information sheet provided to me regarding this study and have had the opportunity to ask questions.

(ii) I understand that my participation in the study is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected.

(iii) I understand that the study staff and the Ethics Committee will not need my permission to look at my health records both in respect of the current study and any further research that may be

conducted in relation to it. I agree to this access. However, I understand that my identity will not be revealed in any information released to third parties or published.

(iv) I agree not to restrict the use of any data or results that arise from this study provided such a use is only for scientific purpose(s).

(v) I agree to take part in the above study.

Participant's Signature: _____

Investigator's Signature: _____

Date: _____/_____/_____

Date: _____/_____/_____

Appendix 3: Proforma for Data collection

DATA SHEET

1. Patient data:

Case	Hosp. No.	Date
Name		Age & sex
Place		

2. Brief clinical data:

Symptoms	
Duration	
Previous surgeries	
Medical treatment	
Previous imaging	

3. Scopy report:

4. Biopsy report:

5. Degree of small bowel distension: (Reference: Masselli G et al, Radiology, May 2016)

Distension score	Axial wall-to-wall diameter - jejunum	Axial wall-to-wall diameter – ileum
0: no distension	No fluid in lumen	No fluid in lumen
1: poor distension	< 20 mm	< 15 mm
2: good distension	20 – 30 mm	15 – 25 mm
3: optimal distension	> 30 mm	> 25 mm

6. Motion artefacts: (Reference: Masselli G et al, Radiology, May 2016)

0	No artefacts
1	Few artefacts
2	Numerous artefacts
3	Non-diagnostic images

7. Mural and extra-mural findings: (Reference: Amitai MM et al, Israeli medical association journal, May 2015)

Findings	Absent	Present. Segment involved / location (MRE)	Present. Segment involved / location (CTE)
Mural thickening (>3mm)			
Mural stratification			
Skip lesions			
Luminal stenosis			
Luminal dilatation			

Phlegmon			
Fistula			
Abscess			
Lymph nodes			
Creeping fat			

8. Were there any complications during the study? Yes / No
9. Extra-intestinal findings if any – soft tissues / joints: Yes / No

Appendix 4: Abbreviations

ABBREVIATIONS:

MRE: magnetic resonance enterography

CTE: computed tomography enterography

IRB: Institutional Review Board

TE: Echo Time

TR: Repetition Time

FSE: fast spin echo

HR: high resolution

FOV: field of view

T – Tesla

ACR: American College of Radiology

CD: Crohn's disease UC:
Ulcerative colitis

TB: Tuberculosis

Appendix 5: Data entry sheet:

Data Sheet

caseno	age	date	sex	place	clindiag	scopy	biopsy	disscore	artefacts	noofseg	murth	murthjej	murthil	murthteril	murthasco
1	30	3/5/2016	1	TN	2	2	1	2	1	2	1	2	2	2	
3	39	3/8/2016	1	AP	4	4	3	1	0	0	2				
4	29	3/10/2016	1	Meghalaya	2	3	3	2	1	0	2				
5	22	3/15/2016	1	Jharkhand	2	1	3	2	1	0	2				
7	27	3/31/2016	1	WB	4	4	3	2	1	1	1	2	2	2	
8	25	4/2/2016	1	WB	3	4	2	1	1	2	1	1	2	2	
13	44	6/7/2016	1	WB	2	4	3	2	1	0	2				
2	27	3/8/2016	1	WB	4	5	4	2	1	3	1	1	1	1	
6	49	3/17/2016	1	WB	2	2	2	1	1	1	1	2	2	1	
9	41	4/13/2016	2	Jharkhand	1	1	2	1	2	3	1	2	1	1	
10	20	4/27/2016	1	Bangladesh	1	1	1	2	1	2	1	1	1	2	
11	18	5/11/2016	1	WB	4	4	3	1	1	1	1	2	2	1	
12	37	6/7/2016	1	WB	1	2	3	1	2	2	1	2	1	1	
14	40	6/15/2016	2	Maharashtra	2	5	4	1	1	1	1	2	2	2	
15	22	6/21/2016	1	WB	4	4	2	1	1	2	1	2	2	2	
16	31	6/24/2016	1	TN	1	1	1	2	1	3	1	2	2	2	
17	22	6/27/2016	1	WB	4	3	2	2	1	3	1	1	1	2	
18	38	6/28/2016	1	WB	1	1	1	2	1	2	1	2	1	1	
19	27	6/30/2016	2	Jharkhand	3	2	1	2	2	3	1	2	1	1	
20	47	7/1/2016	1	Jharkhand	4	4	3	2	1	1	1	2	2	2	
21	47	7/5/2016	1	TN	3	4	4	3	2	2	1	2	2	1	
22	29	7/16/2016	2	Bangladesh	1	2	1	2	1	4	1	2	2	1	
23	40	7/19/2016	1	AP	4	3	3	1	1	3	1	2	2	2	
24	24	7/27/2016	1	Kerala	1	4	4	1	1	2	1	2	2	2	
25	28	7/29/2016	1	Jharkhand	1	2	2	2	1	2	1	2	2	2	

murthrec	murthan	murstr	murstrjej	murstril	murstrteri	murstrasco	murstrtrco	murstrdesc	murstrrs	murstrrec	murstran	skip	skipjej	skipil	skipteril
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		2										2			
		2										2			
2	2	1	2	2	2	2	2	2	1	2	2	2			
1	2	2										1	1	2	2
		2										2			
2	2	2										1	1	1	1
2	2	2										2			
2	2	1	2	1	1	2	2	2	1	2	2	1	2	1	1
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2	2	1	2	2	1	2	2	2	2	2	2	1	2	1	2
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1	2	1	2	2	2	2	2	2	1	1	2	2			
2	1	1	2	2	2	2	1	2	1	2	2	1	2	2	2
2	2	1	1	1	2	2	2	2	1	2	2	1	1	2	2
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2	2	1	2	1	1	1	2	2	2	2	2	2			
2	2	1	2	2	2	2	2	2	1	2	2	2			
1	2	1	2	2	1	2	2	2	2	1	2	2			
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1	2	1	2	2	2	2	1	2	1	2	2	1	2	2	2
2	2	1	2	2	2	2	2	1	1	2	2	2			
2	2	1	2	2	2	2	2	2	1	2	2	1	2	2	2

Skipasco	skiptrcol	skipdesc	skipprs	skipprec	skipan	lumstenn	lumstjej	lumstil	lumstter	lumstasc	lumsttrc	lumstde	slumstrs	lumstrec	lumstan	lumdil	lumdiljej	lumdiljil	lumdilte	lumdilas
						1	2	2	2	2	2	1	2	2	2	2				
						2										2				
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2	2	2	2	1	2	2										2				
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2	2	2	2	2	2	2										1	2	1	2	2
						2										2				
2	2	2	1	2	2	1	2	1	2	2	2	2	1	2	2	1	2	2	2	2
2	2	2	2	2	2	1	2	1	2	2	2	2	2	2	2	1	2	1	2	2
						2										2				
2	2	2	2	2	2	1	2	1	2	2	2	2	2	2	2	2				
						2										2				
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2	1	2	1	2	1	1	2	2	2	2	1	2	1	2	2	2				
2	2	2	2	2	2	1	1	2	2	2	2	2	2	2	2	2				

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2	2	1	1	1	2	2										2				
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2	2	2	1	2	2	1	2	2	2	2	2	2	1	2	2	1	2	2	2	2

lumdiltr	clumdilde	lumdilrs	lumdilre	phlg	fistula	abs	crefat	crefatjej	crefatil	crefatco	lcrefatrs	lyno	ctfinno	mrifinno
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				2	2	2	2					2	0	0
				2	2	2	2					2	0	0
				2	2	2	2					2	0	0
				2	2	2	2					2	1	2
				2	2	2	1	1	2	2	2	2	3	2
				2	2	2	2					2	0	0
2	2	2	2	2	2	2	2					1	3	3
				2	2	2	2					1	2	2
2	2	1	2	2	2	2	2					2	5	5
2	2	2	2	2	2	2	1	2	1	2	2	2	4	5
				2	2	2	2					2	1	2
				2	2	2	2					1	4	3
				2	2	2	2					2	1	1
				2	2	2	1	2	2	2	1	2	2	1
				2	1	1	2					2	5	6
				2	2	2	1	1	2	2	2	1	5	6
				2	2	2	1	2	1	2	2	2	3	3
				2	2	1	2					2	3	3
				2	2	2	2					2	1	2
				2	2	2	1	2	1	2	2	1	4	3
				2	1	2	2					2	4	4
				2	2	1	2					2	4	4
				2	2	1	1	2	2	2	1	2	4	4
2	2	1	2	2	2	2	2					2	4	5

ANEXURE 6 – IRB FORM

OFFICE OF RESEARCH
INSTITUTIONAL REVIEW BOARD
CHRISTIANMEDICALCOLLEGE,
BAGAYAM, VELLORE 632002, TAMIL NADU, INDIA

Ref: FG/9965/03/2016 September 03, 2016

Mr. Robby Pria Sundersingh
The Treasurer
Christian Medical College,
Vellore.

Dear Mr. Robby Pria Sundersingh,

Sub: **Fluid Research Grant NEW PROPOSAL:**
Comparison of MR enterography and CT enterography in patients with Crohn's disease.
Dr. Bernice Thamarai Selvi (Employment Number: 32304), Radiodiagnosis, Dr. Sridhar Gibikote (Employment Number: 14480), Radiodiagnosis , Dr Anu Eapen, Radiodiagnosis, Dr A J Joseph, Gastroenterology.

Ref: IRB Min. No. 9965 dated 02.03.2016

The Institutional Review Board at its meeting held on March 02nd 2016 vide IRB Mtr. No. 9965, Accepted the project for *A sum of 72,950/- INR (Rupees Seventy two Thousand nine hundred and fifty Only) will be granted for 10 Months.*

Kindly arrange to transfer the sanctioned amount to a separate account to be operated by Dr. Bernice Thamarai Selvi (bernice.devarajan@yahoo.com) and Dr. Sridhar Gibikote (gibikote@gmail.com).

Yours sincerely,

Dr. Biju George
Secretary (Ethics Committee)
Institutional Review Board, CMC, Vellore.

Dr. BIJU GEORGE
MBBS., MD., DM.
SECRETARY - (ETHICS COMMITTEE)
Institutional Review Board,
Christian Medical College, Vellore - 632 002

CC: Dr. Bernice Thamarai Selvi, Department of Radiodiagnosis, CMC, Vellore.
Dr. Sridhar Gibikote, Department of Radiodiagnosis, CMC, Vellore.
File.

Dr. B.J. Prashantham, M.A., M.A., Dr. Min (Clinical)
Director, Christian Counseling Center,
Chairperson, Ethics Committee.

Dr. Alfred Job Daniel, D Ortho MS Ortho DNB Ortho.
Chairperson, Research Committee & Principal

Dr. Biju George, MBBS., MD., DM
Deputy Chairperson,
Secretary, Ethics Committee, IRB
Additional Vice-Principal (Research)

Dr. Sathish	MBBS, MD, DCH	Professor, Child Health, CMC, Vellore	Internal, Clinician
Dr. Rekha Pai	MSc, P.hd	Internal Basic Scientist, Int Basic Scientist, CMC, Vellore	External, Legal Expert
Dr. Anand Zachariah	MBBS, PhD	Professor, Medicine, CMC, Vellore	Internal, Clinician

We approve the project to be conducted as presented.

Kindly provide the total number of patients enrolled in your study and the total number of withdrawals for the study entitled: "Comparison of MR enterography and CT enterography in patients with Crohn's disease" on a monthly basis. Please send copies of this to the Research Office (research@cmcvellore.ac.in).

Fund Grant Allocation:

A sum of 72,950/- INR (Rupees Seventy Two thousand nine hundred and fifty only) will be granted for 10 Months. 50,000/- INR (Rupees Fifty Thousand only) will be granted for 5 months as an Ist Installment. The rest of the 22,950/- INR (Rupees Twenty two thousand nine hundred and fifty only) each will be released at the end of the months as 2 nd Installment

Yours sincerely,

Dr. Biju George
Secretary (Ethics Committee)
Institutional Review Board

Dr. BIJU GEORGE
MBBS., MD., DM.,
SECRETARY - (ETHICS COMMITTEE)
Institutional Review Board,
Christian Medical College, Vellore - 632 002.

IRB Min No: 9965 [OBSERVE] dated 02.03.2016

Ethics Committee Blue, Office of Research, 1st Floor, Carman Block, Christian Medical College, Vellore, Tamil Nadu 632 002
Tel: 0416 – 2284294, 2284202 Fax: 0416 – 2262788, 2284481 E-mail: research@cmcvellore.ac.in

Dr. B.J. Prashantham, M.A., M.A., Dr. Min (Clinical)
Director, Christian Counseling Center,
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Chairperson, Research Committee & Principal

Dr. Biju George, MBBS., MD., DM
Deputy Chairperson,
Secretary, Ethics Committee, IRB
Additional Vice-Principal (Research)

Name	Qualification	Designation	Affiliation
Dr. Biju George	MBBS, MD, DM	Professor, Haematology, Research), Additional Vice Principal , Deputy Chairperson (Research Committee), Member Secretary (Ethics Committee), IRB, CMC,Vellore	Internal, Clinician
Dr. Anuradha Rose	MBBS, MD, MHSC (Bioethics)	Associate Professor, Community Health, CMC, Vellore	Internal, Clinician
Dr. Jayaprakash Muliyil	BSc, MBBS, MD, MPH, DCPH (Epid), DMHC	Retired Professor, Vellore	External, Scientist &Epidemiologist
Rev. Joseph Devaraj	BSc, BD	Chaplaincy Department, CMC, Vellore	Internal, Social Scientist
Ms. Grace Rebekha	M.Sc., (Biostatistics)	Lecturer, Biostatistics, CMC, Vellore	Internal, Statistician
Dr. Visalakshi. J	MPH, PhD	Lecturer, Biostatistics, CMC, Vellore	Internal, Statistician
Mrs. Sheela Durai	MSc Nursing	Professor, Medical Surgical Nursing, CMC, Vellore	Internal, Nurse
Dr. Simon Pavamani	MBBS, MD	Professor, Radiotherapy, CMC, Vellore	Internal, Clinician
Mrs. Pattabiraman	BSc, DSSA	Socia. Worker, Vellore	External, Lay Person
Dr. B. J. Prashantham	MA(Counseling Psychol MA(Theology), Dr. Min(Clinical Counselling)	Chairperson, Ethics Committee, IRB, Director, Christian Counseling Cent Vellore	External, Social Scientist
Dr. Rajesh Kannangai	MD, PhD.	Professor, Clinical Virology, CMC, Vellore	Internal, Clinician
Mrs. Emily Daniel	MSc Nursing	Professor, Medical Surgical Nursing, CMC, Vellore	Internal, Nurse

Ethics Committee Blue, Office of Research, 1st Floor, Carman Block, Christian Medical College, Vellore, Tamil Nadu 632 002
Tel: 0416 – 2284294, 2284202 Fax: 0416 – 2262788, 2284481 E-mail: research@cmcvellore.ac.in

OFFICE OF RESEARCH
INSTITUTIONAL REVIEW BOARD (IRB)
CHRISTIAN MEDICAL COLLEGE, VELLORE, INDIA

Dr. B.J. Prashantham, B.A., M.A., Dr. Min (Clinical)
Director, Christian Counseling Center,
Chairperson, Ethics Committee.

Dr. Alfred Job Daniel, D Ortho MS Ortho DNB Ortho
Chairperson, Research Committee & Principal

Dr. Biju George, MBBS., MD., DM
Deputy Chairperson,
Secretary, Ethics Committee, IRB
Additional Vice-Principal (Research)

August 17, 2016

Dr. Bernice Thamarai Selvi,
PG Registrar,
Department of Radiology,
Christian Medical College,
Vellore 632 004.

Sub: **Fluid Research Grant NEW PROPOSAL:**
Comparison of MR enterography and CT enterography in patients with Crohn's disease.

Dr. Bernice Thamarai Selvi (Employment Number: 32304), Radiodiagnosis, Dr. Sridhar Gibikote (Employment Number: 14480), Radiodiagnosis , Dr Anu Eapen, Radiodiagnosis, Dr A J Joseph, Gastroenterology.

Ref: IRB Min No: 9965 [OBSERVE] dated 02.03.2016

Dear Dr. Bernice Thamarai Selvi,

The Institutional Review Board (Blue, Research and Ethics Committee) of the Christian Medical College, Vellore, reviewed and discussed your project titled "Comparison of MR Enterography and CT enterography in patients with Crohn's disease" on March 02nd 2016.

The Committee reviewed the following documents:

1. IRB Application format
2. Consent Forms(Tamil, English, Hindi, Bengali)
3. Information Sheet(Tamil, English, Hindi, Bengali)
4. Proforma
5. Cvs of Drs. Anu Eapen, A J Joseph, Sridhar, Bernice.
6. No. of documents 1 -

The following Institutional Review Board (Blue, Research & Ethics Committee) members were present at the meeting held on March 02nd 2016 in the CREST/SACN Conference Room, Christian Medical College, Bagayam, Vellore 632002.

Ethics Committee Blue, Office of Research, 1st Floor, Carman Block, Christian Medical College, Vellore, Tamil Nadu 632 002
Tel: 0416 – 2284294, 2284202 Fax: 0416 – 2262788, 2284481 E-mail: research@cmcvellore.ac.in

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Additional Vice-Principal (Research)

August 17, 2016

Dr. Bernice Thamarai Selvi.
PG Registrar,
Department of Radiology,
Christian Medical College,
Vellore 632 004.

Sub: **Fluid Research Grant NEW PROPOSAL:**
Comparison of MR enterography and CT enterography in patients with Crohn's disease.

Dr. Bernice Thamarai Selvi (Employment Number: 92304), Radiodiagnosis, Dr. Sridhar Gibikote (Employment Number: 14480), Radiodiagnosis, Dr Anu Eapen, Radiodiagnosis, Dr A J Joseph, Gastroenterology.

Ref: IRB Min No. 9965 [OBSERVE] dated 02.03.2016

Dear Dr. Bernice Thamarai Selvi,

I enclose the following documents:

1. Institutional Review Board approval 2. Agreement

Could you please sign the agreement and send it to Dr. Biju George, Addl. Vice Principal (Research), so that the grant money can be released.

With best wishes,

Dr. Biju George
Secretary (Ethics Committee)
Institutional Review Board

Dr. BIJU GEORGE
MBBS., MD., DM.
SECRETARY - (ETHICS COMMITTEE)
Institutional Review Board,
Christian Medical College, Vellore - 632 002.

Cc: Dr. Sridhar Gibikote, Dept. of Radiodiagnosis, CMC, Vellore

Ethics Committee Blue, Office of Research, 1st Floor, Carman Block, Christian Medical College, Vellore, Tamil Nadu 632 002
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